Newborn Screening Quality Assurance Program

2002 ANNUAL SUMMARY REPORT

Volume 20 February 2003

INTRODUCTION

The Newborn Screening Quality Assurance Program (NSQAP) is designed to help screening laboratories achieve excellent technical proficiency and maintain confidence in their performance while processing large volumes of specimens daily. We continually strive to produce certified dried-blood spot (DBS) materials for reference and quality control (QC) analysis, to improve the quality and scope of our services, and to provide immediate consultative assistance. Through our interactive efforts with the program's participants, we aspire to meet their growing and changing needs. We always welcome comments and suggestions on how we may better serve the newborn screening laboratories.

A major public health responsibility, newborn screening for detection of treatable, inherited metabolic diseases is a system consisting of six parts: education, screening, follow-up, diagnosis, management, and treatment. Effective screening of newborns using dried-blood spot (DBS) specimens collected at birth, combined with follow-up diagnostic studies and treatment, helps prevent mental retardation and premature death. These blood specimens are routinely collected from more than 95% of all newborns in the United States. State public health laboratories or their associated laboratories routinely screen DBS specimens for inborn errors of metabolism and other disorders that require intervention. For more than 24 years, the Centers for Disease Control and Prevention (CDC), with its cosponsor, the Association of Public Health Laboratories (APHL), has conducted research on materials development and assisted laboratories with quality assurance (QA) for these DBS screening tests. The QA services primarily support newborn screening tests performed by state laboratories; however, we also accept other laboratories and international participants into the QA program. All laboratories in the United States that test DBS specimens participate voluntarily in NSQAP. Currently, the program provides QA services for congenital hypothyroidism, phenylketonuria, galactosemia, congenital adrenal hyperplasia, maple syrup urine disease, homocystinuria, biotinidase deficiency, galactose-1-uridyltransferase (GALT) deficiency, and hemoglobinopathies. QA services for cystic fibrosis were added in July 2002.

The QA program consists of two DBS distribution components: QC materials for periodic use and quarterly proficiency testing (PT). The QC program enables laboratories to achieve high levels of technical proficiency and continuity that transcend changes in commercial assay reagents while maintaining the high-volume specimen throughput that is required. The QC materials, which are intended to supplement the participants' method- or kit-control materials, allow participants to monitor the long-term stability of their assays. The PT program provides laboratories with quarterly panels of blind-coded DBS specimens and gives each laboratory an independent external assessment of its performance. DBS materials for QC and PT are certified for homogeneity, accuracy, stability, and suitability for all kits manufactured by different commercial sources.

Over the last seven years, NSQAP has grown substantially, both in the number of participants and in the scope of global participation (Figure 1). In 2002, 310 laboratories in 46 countries (at least one laboratory per country) were active program participants; of these, 210 participated in the PT component and 222 in the QC part (Figure 2). DBS materials for 14 analytes, not including most analytes measured for the separate Tandem Mass Spectrometry (MS/MS) Program, were distributed to participating laboratories (Figure 3). This summary report

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention (CDC)
and the
Association of Public Health Laboratories

NSQAP
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Program Information Web site:
http://www.cdc.gov/nceh/dls/newborn_screening.htm

Data-reporting Web site:
http://www2.cdc.gov/nceh/NewbornScreening

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contains all QC data reported in 2002, including the MS/MS QC data for amino acids and the first QC data for three new analytes: tyrosine (Tyr), valine (Val), and citrulline (Cit). For biotinidase, galactose-1-phosphate uridyltransferase (GALT), and hemoglobins, QC materials were not distributed because of the limited availability of appropriate blood sources.

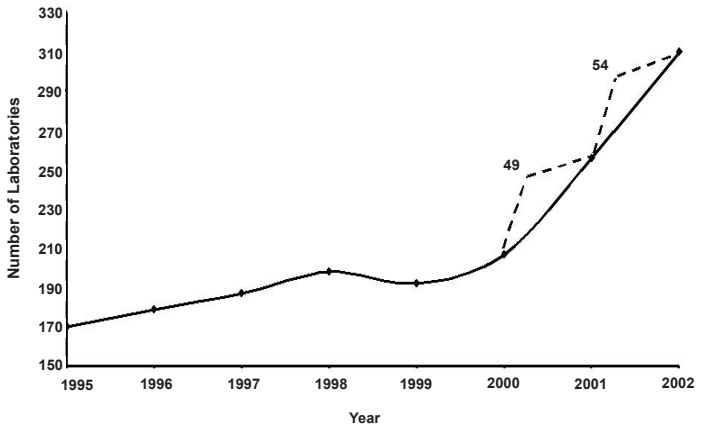
NEW ACTIVITIES

In January 2002, after months of programming and testing, NSQAP officially went "online" with the operation of its paperless data-reporting system whereby global participants can report quarterly PT data over the Internet. In addition, quarterly PT reports for inborn errors of metabolism, biotinidase deficiency, and GALT deficiency panels can be viewed online by participants with user-specific IDs and passwords. The summary data for each quarter beginning in 2002 are available for public view at http://www2.cdc.gov/nceh/NewbornScreening.

In 2001, APHL organized a subcommittee of the Newborn Screening and Genetics in Public Health Committee for quality assurance/quality control/proficiency testing. One mission component of this subcommittee is to provide guidance to the NSQAP on procedures, policies, and activities for the quality assessment of laboratory testing. In January 2002, this subcommittee held its inaugural meeting in Atlanta, where the staff of the NSQAP provided an overall review of their activities. We believe that input from this subcommittee will enhance our continuing efforts to better serve our participants.

The Robert Guthrie Award is given annually to honor a member of the International Society for Neonatal

FIGURE 1. Laboratory Participation in the Newborn Screening Quality Assurance Program, 1995-2002



Screening (ISNS) in worldwide recognition of outstanding contributions to newborn screening. The 1999 Award was given to Dr. W. Harry Hannon, Chief, NSQAP. He received the Award in June, 2002, at the 5th Meeting of the ISNS in Genoa, Italy.

A pilot PT program is underway to serve those laboratories screening newborns for biomarkers of cystic fibrosis. In July 2002, we began distributing panels of DBS for immunoreactive trypsinogen (IRT) measurements in a pilot PT program format. Twenty-one laboratories participated in 2002. We will continue to pursue development of DBS materials for the DNA testing component.

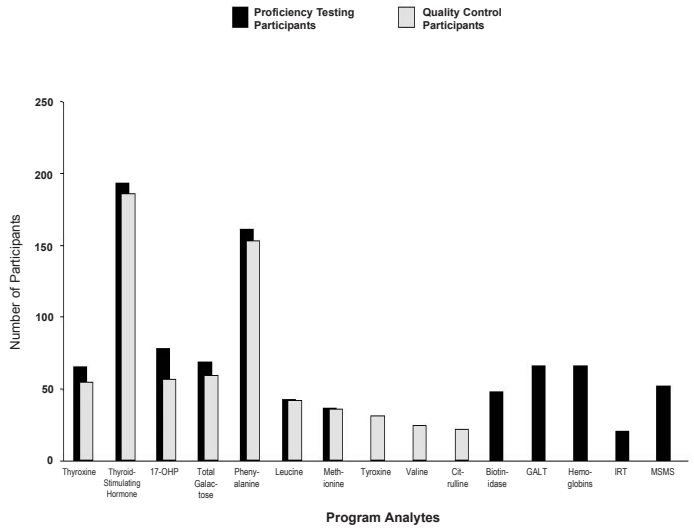
NSQAP cosponsored and helped organize and present the live satellite broadcast, "A New Era in Newborn Screening - Saving Lives, Improving Outcomes," which was aired in September. Four families whose children's lives were saved from life-threatening diseases by newborn screening, early diagnosis, and effective management presented their stories; and a panel of experts explored multiple areas of newborn screening in the United States, from past and current practices to working toward the development of a national agenda.

NSQAP cosponsored and helped organize a workshop, "Banking Newborn Dried Blood Spots for Public Health," on September 23-24, 2002, in Atlanta, Georgia. Fifty physicians and scientists met to develop a strategic plan to assess the feasibility, utility, and practical implementation of a national/multi- state bank of leftover newborn dried blood spots. A publication updating the status of storage of DBS by states and their policies will follow.

In 2002, NSQAP operated a pilot PT program for laboratories testing DBS by tandem mass spectrometry (MS/MS) for detection of amino acid metabolic disorders,

FIGURE 2. Forty-six Countries Participated in the Newborn Screening Quality Assurance Program in 2002

FIGURE 3. Number of Participants in the Newborn Screening Quality Assurance Program, 2002



**Quality control materials are not available because of limited sources for donor blood.*

urea cycle disorders, fatty acid oxidation disorders, and organic acid metabolic disorders. In Quarter 4, we added a presumptive-classification grading component to the MS/MS PT program for amino acids. We plan to bring the MS/MS PT program for acylcarnitines to evaluation status in 2003.

In October 2002, NSQAP released a report, "Genetic Risk for Type 1 Diabetes Using Dried-Blood Spots," which describes the evaluation/validation of a specimen library proposed for PT. Six research laboratories that do population-based testing participated in the evaluation. In 2003, we plan to distribute five-specimen panels composed of spots from the validated-specimen library in a Type 1 Diabetes pilot PT program.

A presumptive-classification grading component was added to the MS/MS PT program for amino acids.

NSQAP cosponsored and helped organize a symposium, "Challenges for the Future: Newborn Screening State Policies and Procedures," on November 21-24, 2002, at the University of California, Los Angeles. This symposium was designed (1) to explore, innumerate, and compare the existing state legislation and code governing newborn screening among the 50 states and territories,

Front Row: Sharon McNeely, Sherri Hall, Jarad Schiffer, Joanne Mei, Lixia Li, Hugh Gardner. Second Row: Carol Bell, Anand Swamy, Elizabeth McCown, Harry Hannon. Back Row: Bob Vogt, Connie Singleton, Marie Earley, Sarah Brown, Tim Lim, Dimitri Fillos, Barbara Adam, Nancy Meredith.
Absent: Omar Henderson, Paul Dantonio, Lisa Kalman.

(2) discuss the policies and procedures for storage and use of leftover blood spots, and (3) discuss the policies and procedures for the process of informed consent and retention and use of leftover blood spots. Approximately 100 invited public health professionals, lawyers, and ethics experts attended.

The National Center for Environmental Health's annual awards ceremony was held October 3, 2002. The Director's Award for Superior Mission Response - Science (Group) was presented to the "*Newborn Screening Quality Assurance Program for outstanding mission achievements as sole provider of comprehensive performance evaluation services and research to screening laboratories worldwide."* Our hard-working group was happy to receive the honor.

In 2002, NSQAP had 87 participants from Spanish-speaking countries. The Spanish translations of the major documents that describe the proficiency testing and quality control schemes were reviewed and validated for accuracy. We began a new project to translate the data-entry instructions for the NSQAP data-reporting Web site into Spanish. Two NCEH scientists, a Castilian Spanish-speaker and a Latin American Spanish-speaker, collaborated with the CDC en Español translator to validate the translation. The new data-reporting Web site instructions document will be available in early 2003.

In July, 2003, NSQAP will celebrate its 25th anniversary of service to newborn screening laboratories around the world. We continually strive to improve the scope of our services and to meet the growing and changing needs of our participants. We have grown from eight domestic participants testing for one disorder in 1978 to over 300 worldwide participants testing for more than 30 disorders today.

FILTER PAPER

The paper disk punched to aliquot DBS specimens is a volumetric measurement and requires a degree of uniformity among and within production lots. As part of the QA program, we used an isotopic method[1] developed at CDC to evaluate and compare different lots of filter paper. Mean counts per minute of added isotopic-labeled T_4 within a 1/8-inch disk were equated with the serum volume of the disks from the dried whole blood specimens. In comparing production lots, we used statistical analyses of the counting data to determine values for homogeneity and serum absorption of the disks. To avoid the variability contributed by uncontrolled red blood cell (RBC) lysis, we initially used lysed-cell whole blood for variance studies with filter paper. The results of later studies have indicated that RBC lysis during the process is not sufficient to contribute substantially to the variance; however, the mean serum volume per disk is different with intact-cell blood. For historical reference and for maintaining uniformity of testing on all the paper production lots, we have continued using the lysed-cell procedure. We also measure performance with intact-cell preparations. The published and standardized acceptable volumes per 1/8-inch disk are 1.30 ± 0.19 µL (mean value and 95% confidence interval) for lysed-cell blood and 1.54 ± 0.17 µL for intact-cell blood.[1] As shown in Figures 4-7, the mean values and confidence intervals (CI) are the filter-paper evaluation parameters published in the NCCLS approved standard.[1] As shown in Figures 5 and 7, the second mean value (solid line) is the mean value produced from the NSQAP database. This year, the line was added for reference. The mean values for all lots are within the 95% CI defined by NCCLS but are below the mean values indicated by the NCCLS standard.[1]

In 2002, the mean value and CI for the intact cell measurements were examined and discussed during the routinely scheduled review period for revision of the NCCLS standard. The NCCLS committee decided to retain the original values, which were not produced at CDC, in the revised standard. Soon NSQAP will have accumulated sufficient data for intact cell measurements among lots to calculate a mean value and CI for intact cell assessments of different lots. In future summary reports, our mean value and CI will be included in the figures.

Filter paper lots used in the CDC production of QC and PT specimens distributed in 2002 were W981 and W001 of Grade 903. All filter paper lots were analyzed for agreement with the evaluation parameters according to the NCCLS approved standard.[1]

Each year, with the extensive cooperation of manufacturers (Schleicher & Schuell and Whatman) of filter papers approved by the Food and Drug Administration (FDA) for blood collection, we have conducted routine evaluations of new lots and compared new lots with previous lots. The criteria for acceptable performance are the approved limits established in the NCCLS standard.[1] Each manufacturer is also expected to establish its own testing program using the NCCLS standard and make available to the user its certification data for each distributed lot of paper. The independent evaluations by CDC are an impartial and voluntary service offered as a function of our quality assurance program and do not constitute preferential endorsement of any product over other specimen collection papers approved by the FDA.

Filter paper lots used in the CDC production of QC and PT specimens distributed in 2002 were W981 and W001 of Grade 903.

The serum-absorbance volumes of 19 lots of Grade 903 filter paper (Schleicher & Schuell, Keene, NH) determined from lysed-RBC blood and for 9 lots determined from intact-RBC blood, are shown in chronological order. For W011, the most recent production lot of Grade 903 filter paper, we found the mean serum-absorbance volume to be 1.45 µL for a 1/8-inch disk for lysed-cell blood and 1.57 µL per 1/8-inch disk for intact-cell blood. Each mean value is within the acceptable range for the matrix used. Lot W011 was homogeneous (i.e., the measured within-spot, within-sheet, and among-sheets variances were within the acceptable limits).

In 1996, the FDA approved the filter paper, BFC180, produced by Whatman Inc. (Fairfield, NJ) as a blood collection device. The BFC180 was evaluated by CDC according to the criteria previously described.[1] The serum-

FIGURE 4. Schleicher and Schuell Grade 903 Filter Paper Serum Volume by Lot Number - Lysed Red Blood Cells

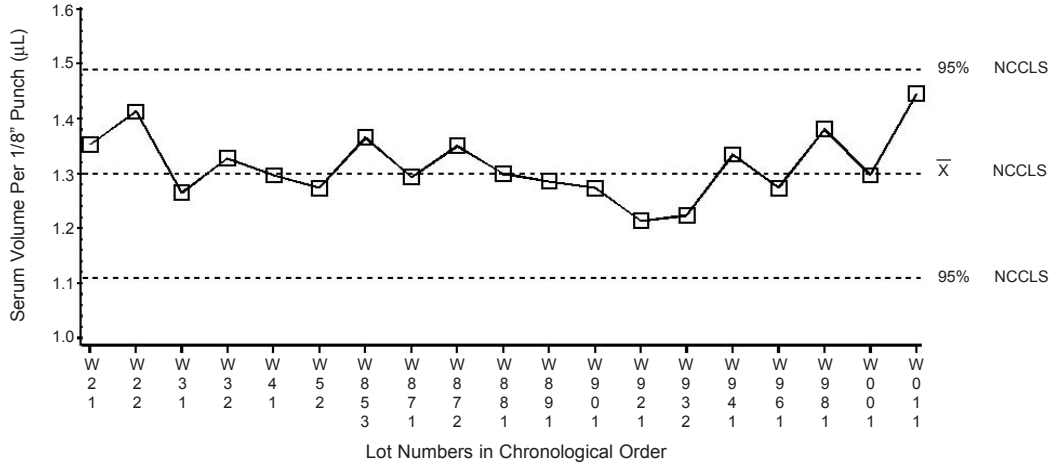
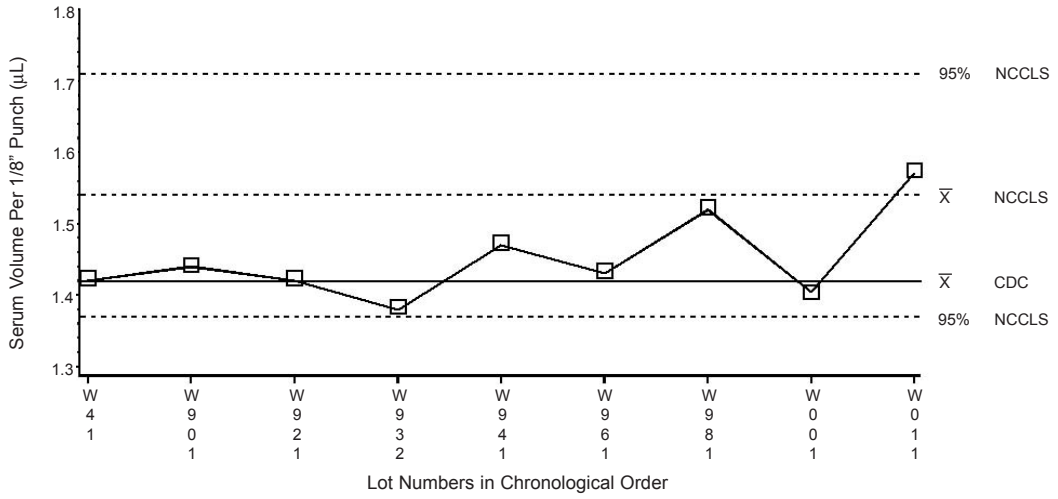


FIGURE 5. Schleicher and Schuell Grade 903 Filter Paper Serum Volume by Lot Number - Intact Red Blood Cells



absorbance volumes for eight lots of BFC180 filter paper determined from lysed- RBC blood and determined from intact-RBC blood, are shown in chronological order. For 1488, the most recent production lot of BFC180 filter paper, we found the mean serum-absorbance volume to be 1.37 µL for a 1/8-inch disk for lysed-cell blood and 1.51 µL per 1/8-inch disk for intact-cell blood. Each mean value is within the acceptable range for the matrix used. Lot 1488 was homogeneous (i.e., the measured within-spot, within-sheet, and among-sheets variances were within the acceptable limits).

SPECIMEN PREPARATION AND DATA HANDLING

Tables and figures show the enriched concentrations of all PT specimens and QC lots as well as the summarized quantitative data. The total concentration of each specimen or lot was equal to the sum of the enriched concentration and the endogenous concentration (nonenriched). For T_4 PT specimens, the CDC assayed values were reported because of differences in the blood sources used for DBS production. Some specimens were enriched above the endogenous T_4 concentration, and some were

FIGURE 6. Whatman BFC180 Filter Paper
Serum Volume by Lot Number - Lysed Red Blood Cells

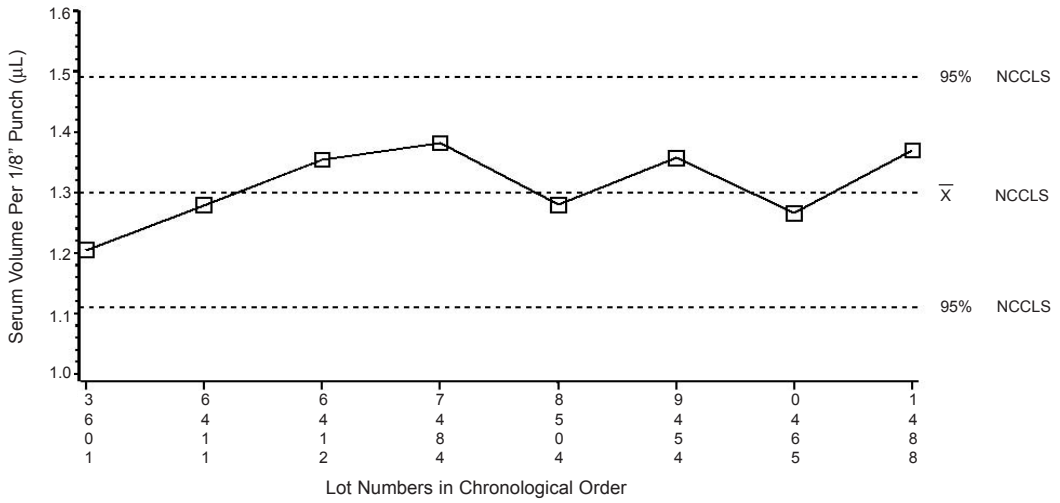
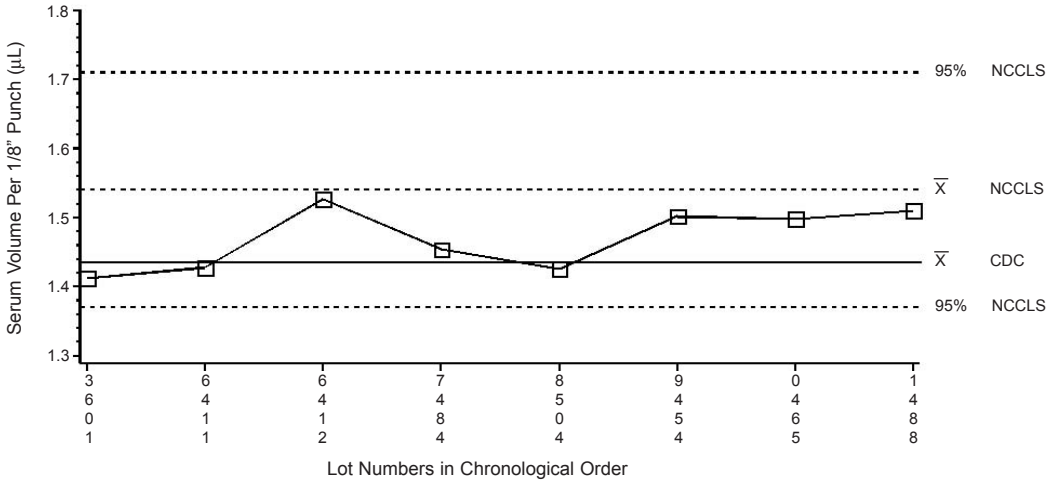


FIGURE 7. Whatman BFC180 Filter Paper
Serum Volume by Lot Number - Intact Red Blood Cells



enriched with T_4 after T_4 depletion of the base serum. Except for biotinidase and GALT, all DBS specimens in the PT surveys and QC production lots were prepared from whole blood of 55% hematocrit. Purified analytes or natural donor blood, except for TSH, which used the Second International Reference Preparation (80/558), were used for all enrichments. For galactosemia, enrichments were made with galactose, galactose-1-phosphate, or both so that both free galactose (galactose alone) and total galactose (free galactose plus galactose present as galactose-1-phosphate) could be measured. For biotinidase and GALT, individual donor blood, with hematocrit adjusted to 50%, was used. All reported analytic values outside the 99% confidence limits were excluded from the summaries of quantitative results.

For obtaining data on the QC materials, we estimated the method response to endogenous materials by performing weighted linear regression analyses for mean-reported concentrations versus enriched concentrations. We then extrapolated the regression lines to the Y-axis to obtain an estimate of the observed endogenous analyte concentration for each method category. These estimates are reliable when (1) enrichments are accurate, (2) the analytic

method gives a linear response across the range of the measurements, and (3) the slopes for regression lines are approximately equal to one.

In 2002, we applied the laboratory-reported specific cutoff values, when available, to our judgment algorithm for clinical assessments; otherwise, we used the NSQAP-assigned working cutoff values that are based on the national mean value for this assessment.

CUTOFFS

When reporting cutoff values, we requested the decision level for sorting test results that are reported as presumptive positive (outside limits) from results reported as negative (within limits).

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FIGURE 8a. Cutoff Values for Domestic and Foreign Laboratories by Analyte

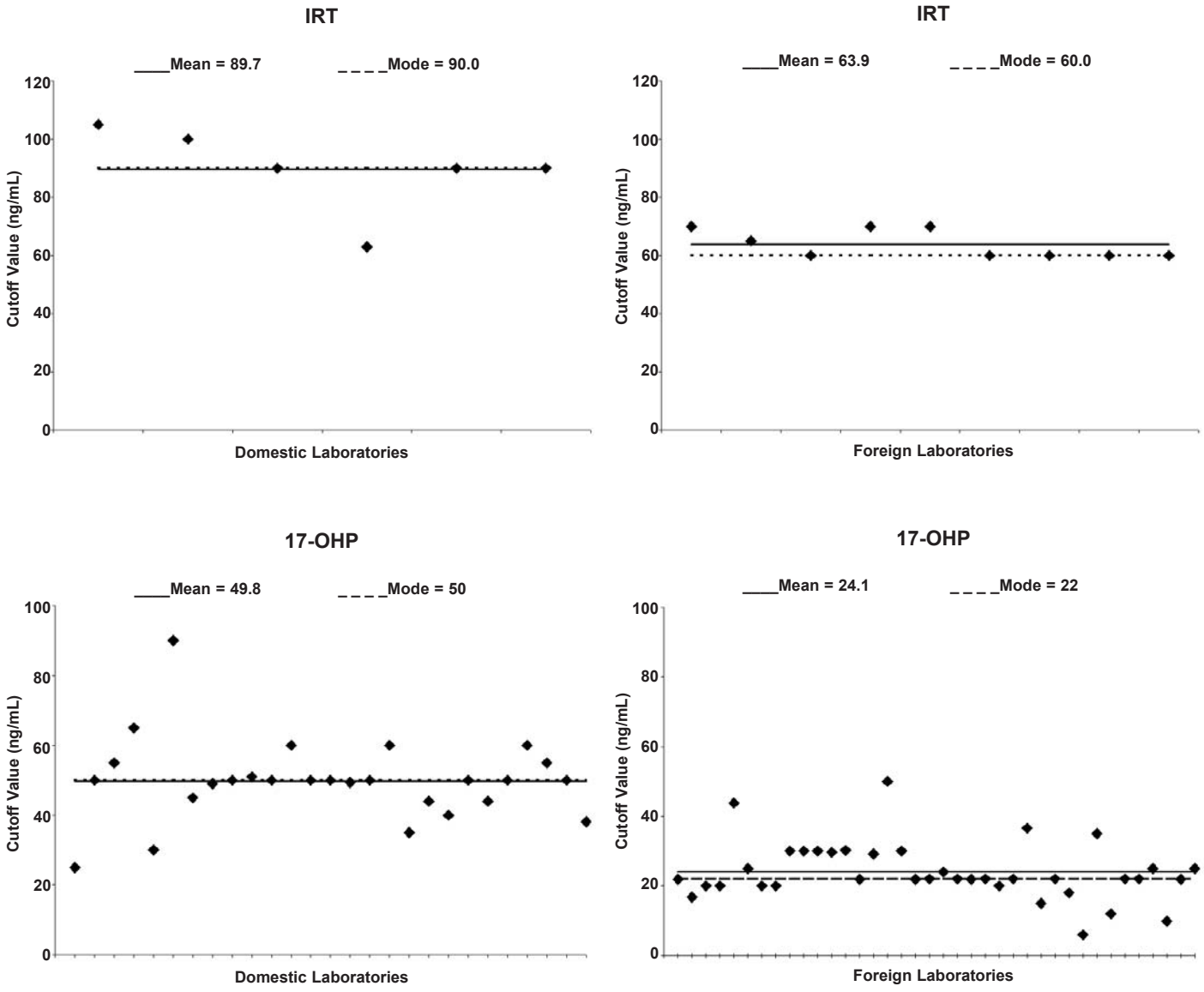
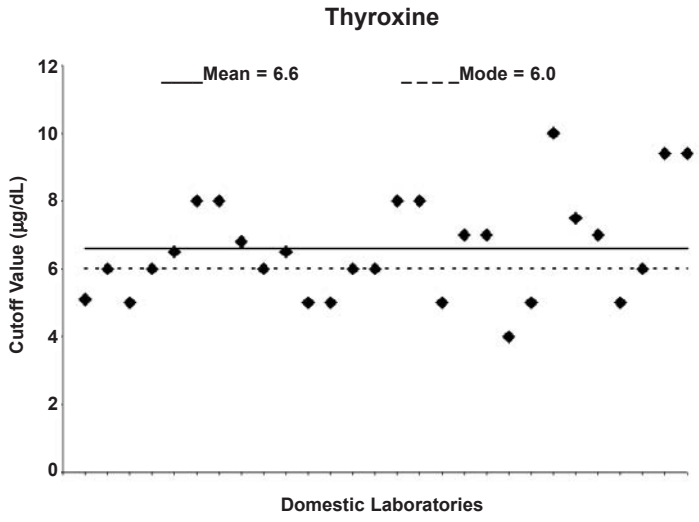
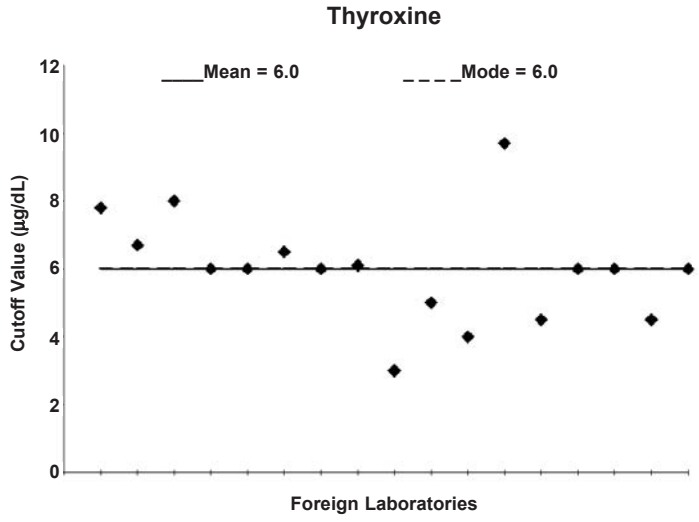
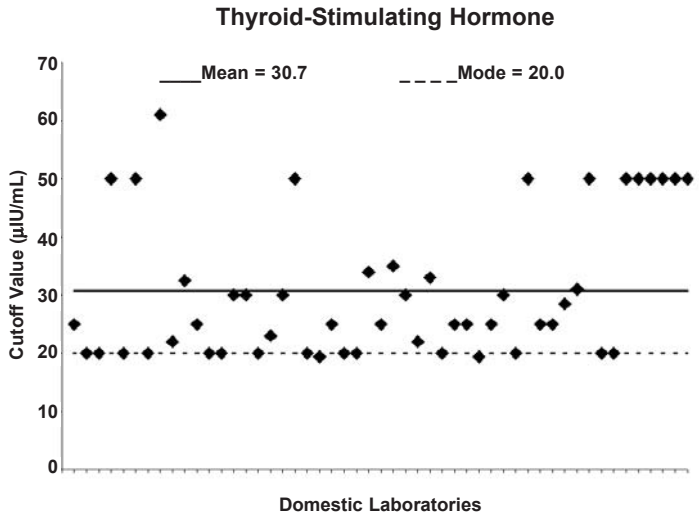
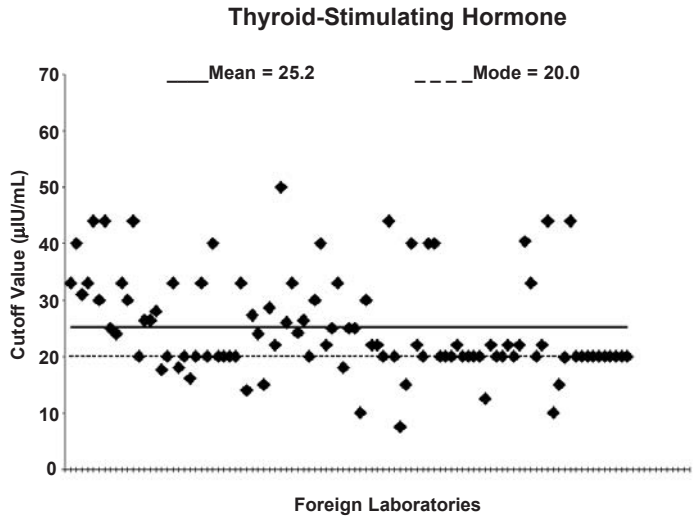


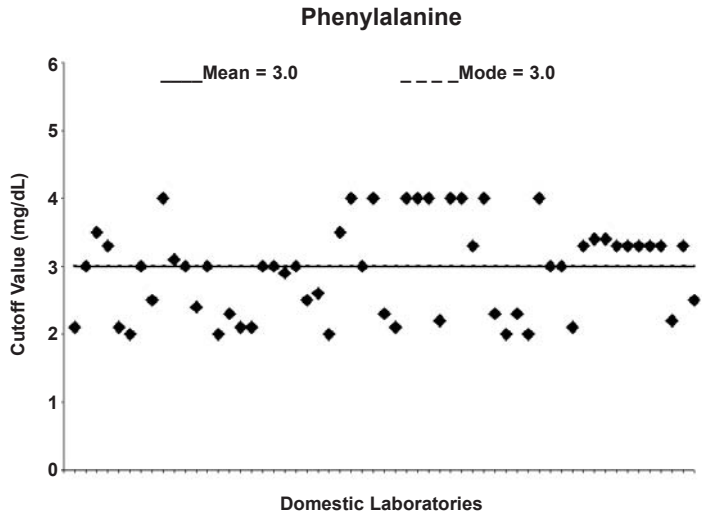
FIGURE 8b. Cutoff Values for Domestic and Foreign Laboratories by Analyte











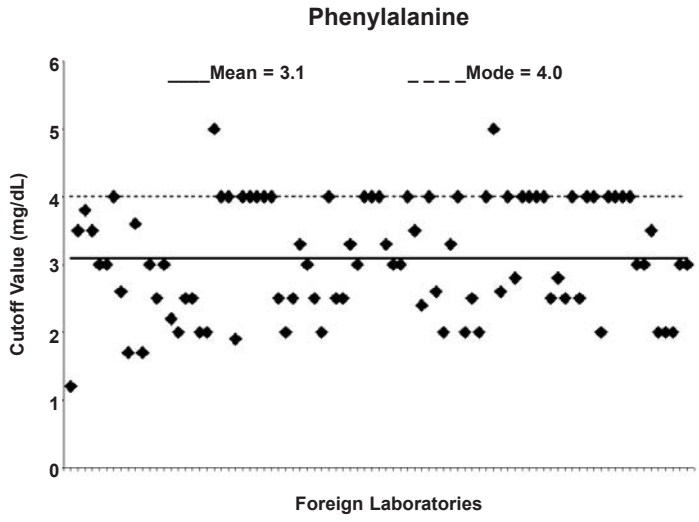
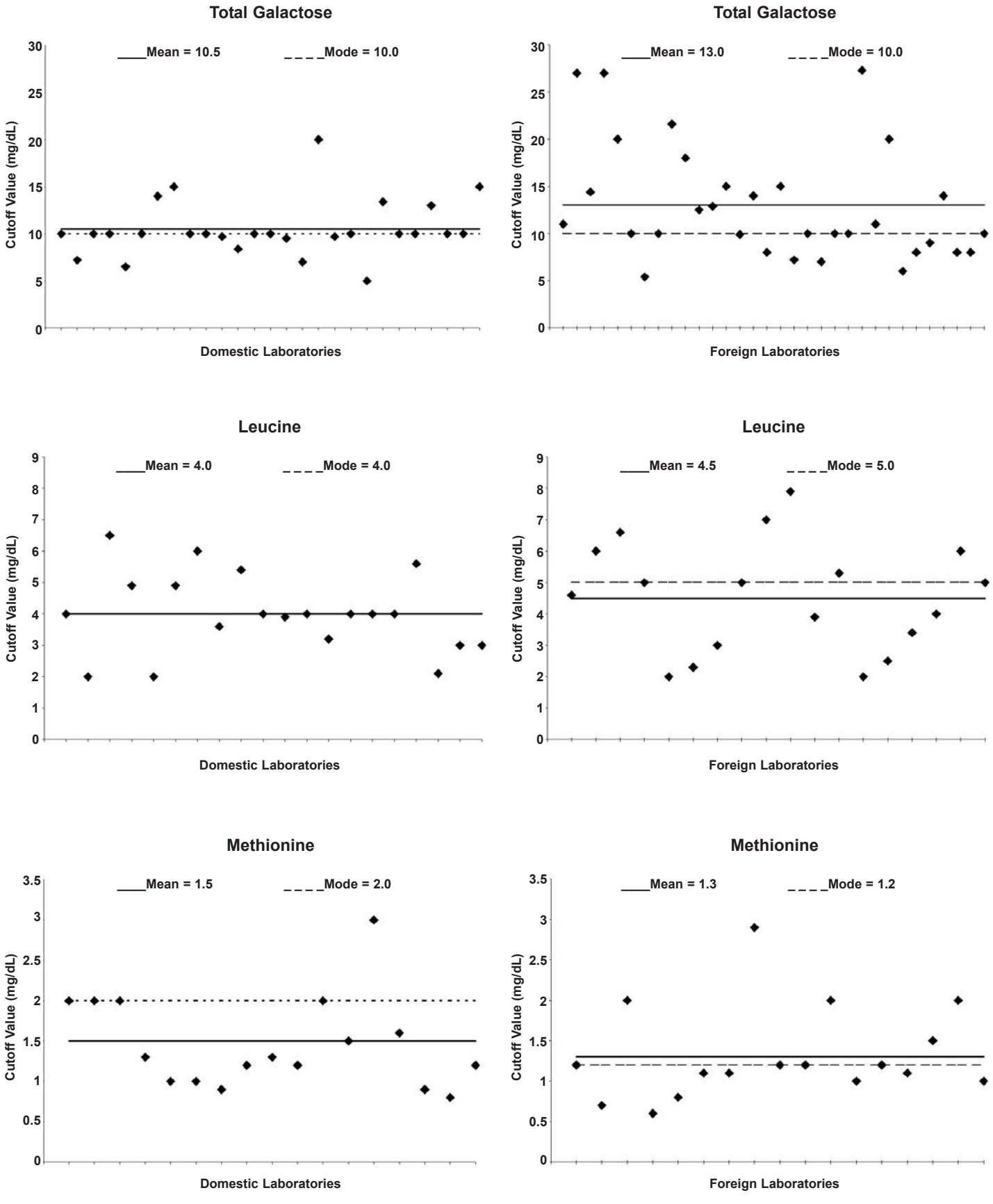


FIGURE 8c. Cutoff Values for Domestic and Foreign Laboratories by Analyte



ative (within limits). The cutoff values shown in Figures 8a-8c illustrate the distribution of reported cutoffs for domestic and foreign laboratories. The values for the mean (arithmetic average) and the mode (most frequent value) are shown for each analyte. The mean cutoff values for domestic and foreign laboratories were similar except those for 17-OHP, which were twice as high for domestic laboratories. The cutoff values for IRT (Figure 8a) are 30% higher for domestic laboratories than for foreign laboratories. The scatter of cutoff values for total galactose (Figure 8c) is larger for foreign laboratories than for domestic laboratories. The cutoff values for Phe and TSH for both domestic and foreign laboratories show a large scatter around the mean value. This observation is somewhat surprising because Phe and TSH are the most common and historical analytes in newborn screening. For domestic laboratories, the Phe mean and mode values are the same.

The most common reason for a false-negative error is a low quantitative value.

PROFICIENCY TESTING

All PT panels contained five blind-coded 100-µL DBS specimens. Specimens in the PT panels contained either endogenous levels or were enriched with predetermined levels of thyroxine (T_4), thyroid- stimulating hormone (TSH), phenylalanine (Phe), total galactose (Gal), 17 α-hydroxyprogesterone (17- OHP), leucine (Leu), and methionine (Met). Specimens for the cystic fibrosis panel were prepared with IRT enriched blood. Special separate panels for biotinidase deficiency and for GALT deficiency were prepared with purchased blood from donors with enzyme deficiencies. Specimens for the hemoglobinopathies panel were prepared from umbilical cord blood.

Specimen sets were packaged in a zip-close metallized plastic bag with desiccant, instructions for analysis, and data-report forms for those laboratories that did not report data by Internet. We prepared and distributed quarterly reports of all results that had been received by the cutoff dates. In this annual report, Figures 9-24 for reproducibility of results by different methods summarize the data for PT specimens that were sent multiple times within an event or among events. The time intervals are within quarter or among quarters. Also, a summary of the specimen data for all PT challenges in 2002 is tabulated in the left margin. The expected presumptive clinical assessments are included for each specimen illustrated in the reproducibility plots except for thyroxine, which is assessed in tandem with TSH and not alone. For reference, see the scatter of reported cutoff values for a specific analyte in Figures 8a-8c. One of the total galactose specimens (Figure 15) falls into a not-evaluated (NE) category, i.e., specimens containing analyte concentrations that are near the cutoff value and subject

TABLE 1. 2002 Summary of Performance Evaluation Errors by Domestic and Foreign Laboratories

Domestic	Positive Specimens Assayed (N)	False-Negative Errors (%)	Negative Specimens Assayed (N)	False-Positive Errors (%)
Hypothyroidism	456	2.2	457	2.4
Phenylketonuria	470	0.9	589	0
Galactosemia	210	0	289	3.4
Congential Adrenal Hyperplasia	243	0.4	297	0
Maple Syrup Urine Disease	158	2.5	198	2.0
Homocystinuria	168	5.4	133	0
Biotinidase Deficiency	84	0	336	0
GALT Deficiency	181	0	724	0.7
Cystic Fibrosis (IRT) - Pilot Phase	38	13.2	37	0
Foreign	**Positive Specimens Assayed (N)**	**False-Negative Errors (%)**	**Negative Specimens Assayed (N)**	**False-Positive Errors (%)**
Hypothyroidism	588	2.4	667	4.2
Phenylketonuria	658	1.8	821	1.2
Galactosemia	244	1.2	338	1.8
Congential Adrenal Hyperplasia	300	0.3	390	4.9
Maple Syrup Urine Disease	151	1.3	187	3.7
Homocystinuria	181	3.9	143	5.6
Biotinidase Deficiency	81	2.5	324	1.9
GALT Deficiency	55	1.8	220	4.5
Cystic Fibrosis (IRT) - Pilot Phase	43	0	47	8.5

to different interpretations. For some analytes, no within- or among-quarter data are available. In these cases, only a method comparison is presented. Only the qualitative assessments are reported for the PT surveys for (1) sickle cell disorders and other hemoglobinopathies, (2) biotinidase deficiency PT surveys, and (3) PT surveys for GALT deficiency. Presumptive clinical classifications (qualitative assessments) of some specimens may differ by participant because of specific clinical assessment practices. If participants provided us with their cutoff values, we applied these cutoffs in our final appraisal of the error judgment.

In general, the quantitative reproducibility (Figures 9-24) for PT challenges is good within a method but varies among methods. The PT quantitative results are grouped by kit or method to illustrate any method-related differences in analyte recoveries. Because some of the pools in a routine PT survey represent a unique donor specimen, differences in endogenous materials in the donor specimens may influence method-related differences. The T_4 and TSH results (Figures 9-12) show a reasonably consistent performance among the different methods, with three methods showing slightly higher values for T_4 and two methods slightly higher for TSH. For Phe (Figures 17-18), the reported results show reasonable variability among methods, except for one method that shows higher values. The among-method comparisons of mean values for most methods appear reasonable for 17-OHP and Gal (Figures 13-16) except for two Gal methods, one that gave low values and one that shows poor reproducibility. One method for total galactose, which was from the same source that produced high values for Phe, produced values higher than those of most other methods. The reproducibility and recoveries for Phe were good for most methods when both enrichment and endogenous concentrations were weighted in the assessment. The recovery values reported for Leu (Figures 19-20) show variability at the low concentration and better comparability at the higher level. One method for Met (Figures 21-22) produced higher values than the others, but within-method reproducibility was good for all methods. For IRT (Figures 23-24), the reported results show good reproducibility within methods; but one method shows high recoveries at higher concentrations and the "Other" method shows low recovery and poor reproducibility.

TABLE 2. Summary of Performance Evaluation Errors for Hemoglobinopathies by Domestic and Foreign Laboratories

Hemoglobinopathies	Domestic	Foreign
Specimens assayed	1015	265
Phenotype errors	0.1%	0%
Clinical assessment errors	0.1%	0.8%

Table 1 shows the performance evaluation errors reported by disorder in 2002 for all qualitative assessments by domestic laboratories and by foreign laboratories. We applied the laboratory-reported specific cutoff values to our judgment algorithm for clinical assessments (see "Cutoffs" section). The rates for false-positive misclassifications were based on the number of distributed negative specimens, and the rates for false-negative misclassifications were based on the number of positive specimens. False-positive misclassifications, which are a cost-benefit issue and a credibility factor for follow-up programs, should be monitored and kept as low as possible. Many of the misclassifications were in the false-positive category, with false-positive rates ranging from 0% to 8.5%. For domestic laboratories, the rate was 2.4% or lower for eight of nine disorders; and for foreign laboratories, the rate was 4.5% or greater for seven of nine disorders. Screening programs are designed to avoid false-negative reports; this precautionary design, however, contributes to false-positive reports and may be the cause of many of the false-positive misclassifications. The false-negative rate, expected to be zero, ranged from 0% to 5.4%, not including 13.5% for the pilot cystic fibrosis (IRT) program. False-negative classifications were reported for the eight disorders, with the highest rate reported for homocystinuria. For three disorders, no false-negative errors were reported for the domestic laboratories. A few of our PT specimens fell close to the decision level for classifica-

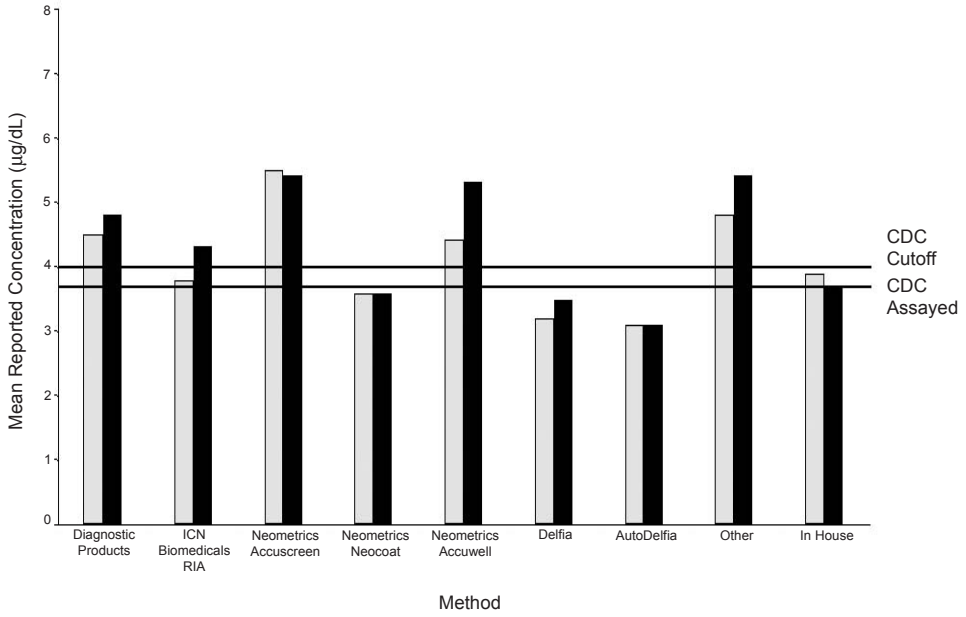
TABLE 3. Most Common Reasons for False-Negative Errors Reported by Domestic Laboratories

Low quantitative value	75.0%
Transcription error	14.3%
Analytic testing error	3.6%
Other	7.1%

FIGURES 9-10. Reproducibility of Results by Different Methods - Thyroxine

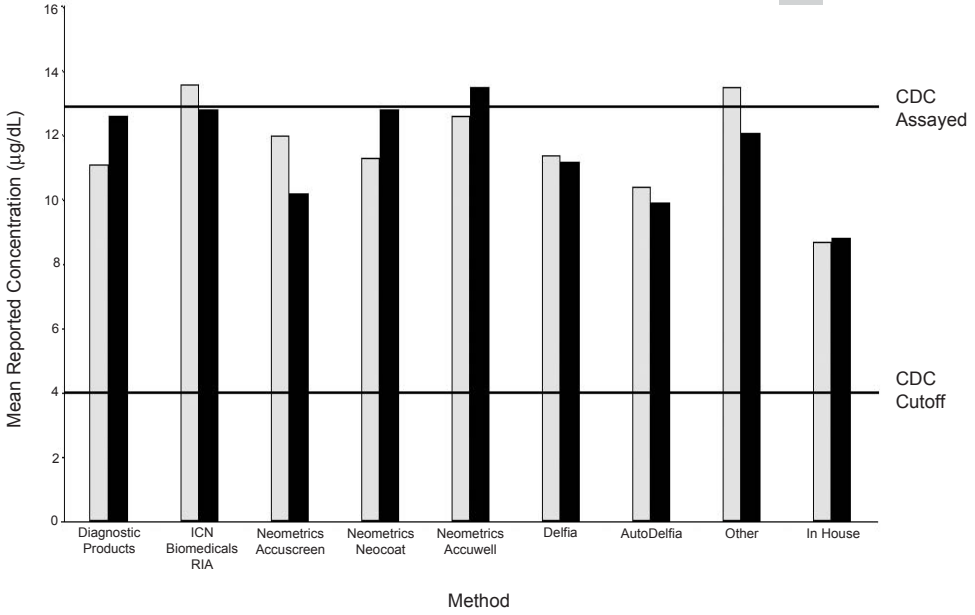
	Quarter 1	Quarter 2
Specimens		
Enriched	4	5
CDC Assayed	12.1	14.4
Reported Mean	13	13.2
Specimens		
Enriched	5	3
CDC Assayed	10.2	5.3
Reported Mean	9.8	4.2
Specimens		
Enriched	3	3
CDC Assayed	3.7	3.7
Reported Mean	4	3.5
Specimens		
Enriched	5	5
CDC Assayed	12.9	12.9
Reported Mean	11.3	11.1
Specimens		
Enriched	5	3
CDC Assayed	15.2	3.7
Reported Mean	12.9	3.6

Figure 9. Thyroxine Within Quarter Results



	Quarter 3	Quarter 4
Specimens		
Enriched	4	4
CDC Assayed	5.3	12.7
Reported Mean	4.3	10.3
Specimens		
Enriched	4	4
CDC Assayed	11.6	5.3
Reported Mean	8.9	4.1
Specimens		
Enriched	4	4
CDC Assayed	3.3	3.3
Reported Mean	3.4	2.9
Specimens		
Enriched	4	4
CDC Assayed	3.1	10
Reported Mean	3.2	8.4
Specimens		
Enriched	4	4
CDC Assayed	12.7	7
Reported Mean	11	6.1

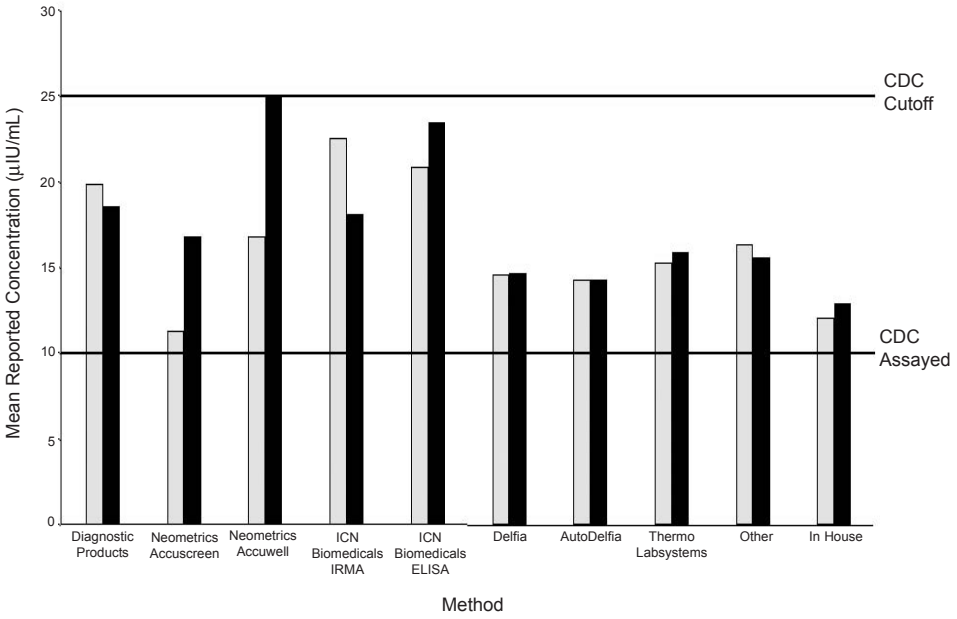
Figure 10. Thyroxine Among Quarter Results



FIGURES 11-12. Reproducibility of Results by Different Methods - Thyroid-Stimulating Hormone

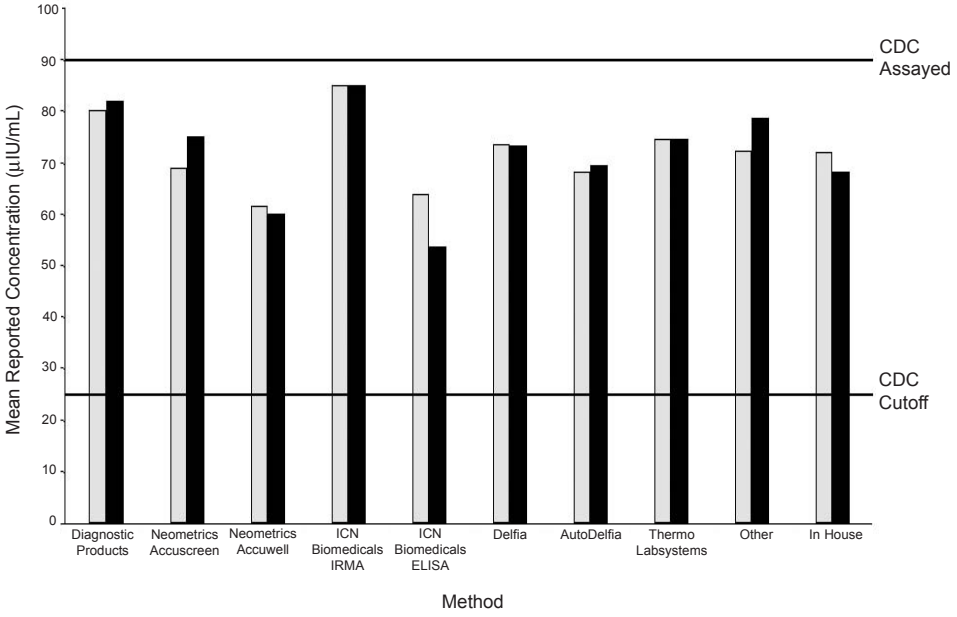
	Quarter 1	Quarter 2
Specimens		
Enriched	12	11
CDC Assayed	17	12
Reported Mean	19.1	14.3
Specimens		
Enriched	9	70
CDC Assayed	6	85
Reported Mean	11	82.3
Specimens		
Enriched	65	65
CDC Assayed	72	72
Reported Mean	75.9	74.6
Specimens		
Enriched	10	10
CDC Assayed	10	10
Reported Mean	15.1	15
Specimens		
Enriched	10	65
CDC Assayed	7	72
Reported Mean	11.7	74.2

Figure 11. Thyroid-Stimulating Hormone Among Quarter Results
Presumptive Clinical Assessment = Negative



	Quarter 3	Quarter 4
Specimens		
Enriched	75	9
CDC Assayed	90	4
Reported Mean	70.9	8.9
Specimens		
Enriched	10	75
CDC Assayed	7	90
Reported Mean	9.9	72.1
Specimens		
Enriched	60	60
CDC Assayed	57	57
Reported Mean	60.7	60.7
Specimens		
Enriched	75	10
CDC Assayed	65	10
Reported Mean	77.8	13.5
Specimens		
Enriched	9	9
CDC Assayed	4	9
Reported Mean	9	9.9

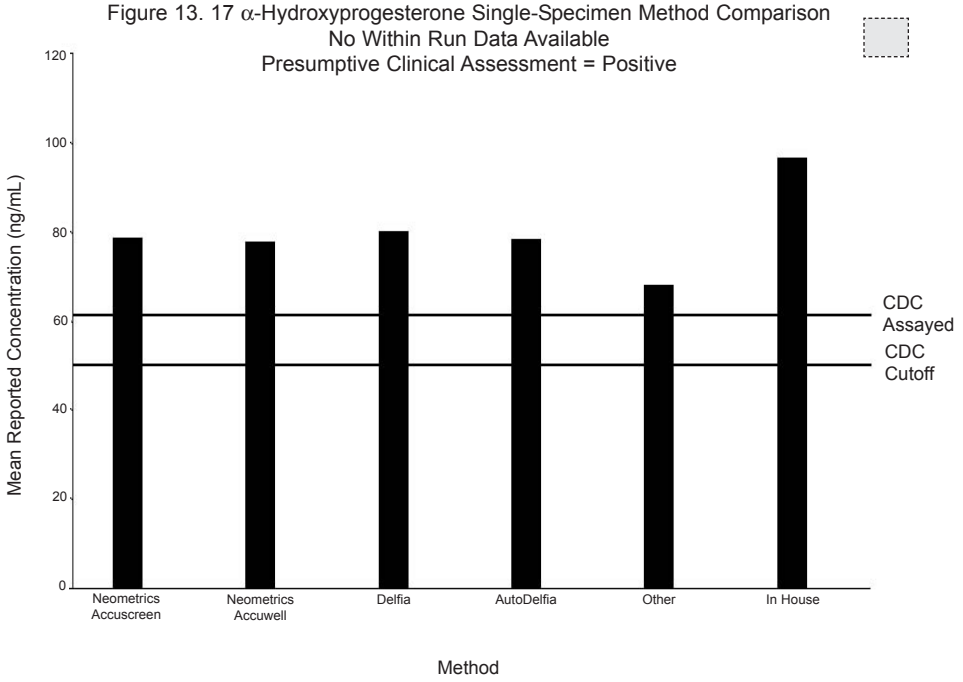
Figure 12. Thyroid-Stimulating Hormone Among Quarter Results
Presumptive Clinical Assessment = Positive



FIGURES 13-14. Reproducibility of Results by Different Methods - 17 α-Hydroxyprogesterone

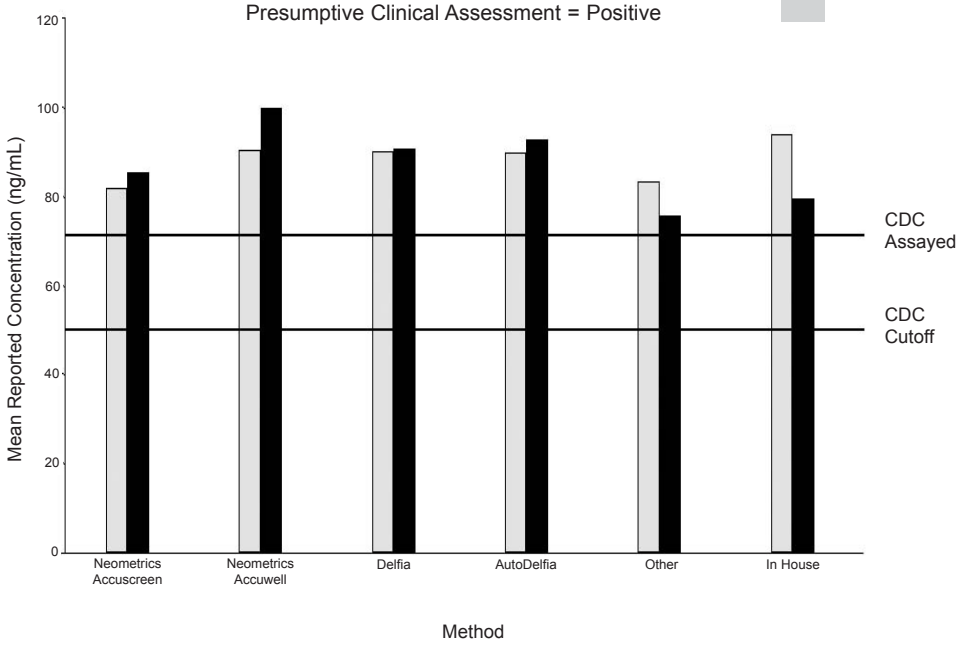
	Quarter 1	Quarter 2
Specimens		
Enriched	150	10
CDC Assayed	133	17
Reported Mean	158.3	19.1
Specimens		
Enriched	60	5
CDC Assayed	90	5
Reported Mean	104.9	1.2
Specimens		
Enriched	60	60
CDC Assayed	93	93
Reported Mean	112.7	112.5
Specimens		
Enriched	0	0
CDC Assayed	3.2	3.2
Reported Mean	6	6
Specimens		
Enriched	6	60
CDC Assayed	13	93
Reported Mean	13.9	112.6

Figure 13. 17 α-Hydroxyprogesterone Single-Specimen Method Comparison
No Within Run Data Available
Presumptive Clinical Assessment = Positive



	Quarter 3	Quarter 4
Specimens		
Enriched	5	75
CDC Assayed	5	71.4
Reported Mean	6.2	89.7
Specimens		
Enriched	75	5
CDC Assayed	70	5
Reported Mean	84.8	6.5
Specimens		
Enriched	5	5
CDC Assayed	7.1	7.1
Reported Mean	10.2	10.6
Specimens		
Enriched	65	5
CDC Assayed	61.2	16.4
Reported Mean	77.5	18.7
Specimens		
Enriched	75	0
CDC Assayed	71.4	0
Reported Mean	89	2.9

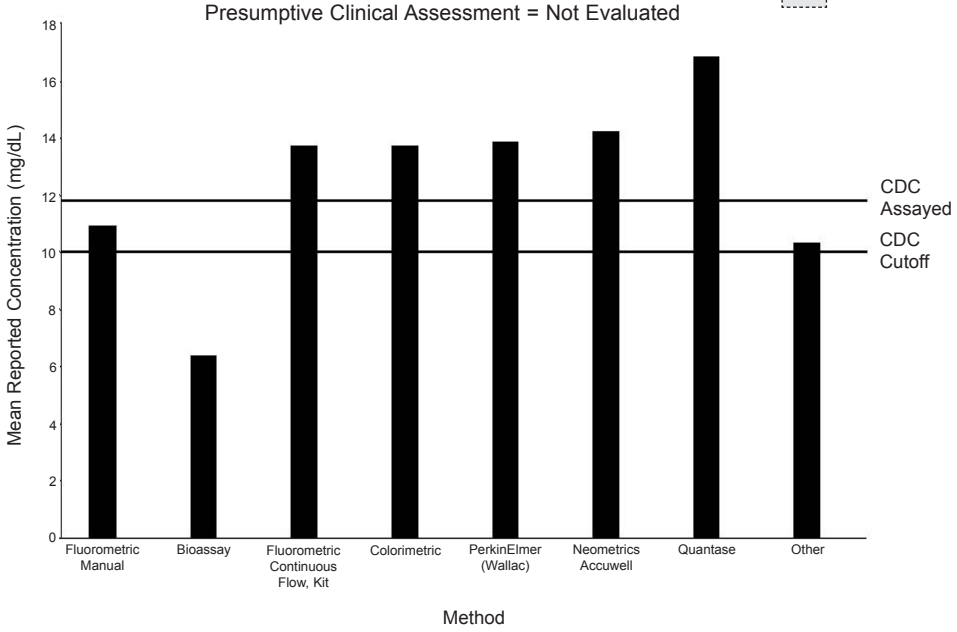
Figure 14. 17 α-Hydroxyprogesterone Among Quarter Results
Presumptive Clinical Assessment = Positive



FIGURES 15-16. Reproducibility of Results by Different Methods - Total Galactose

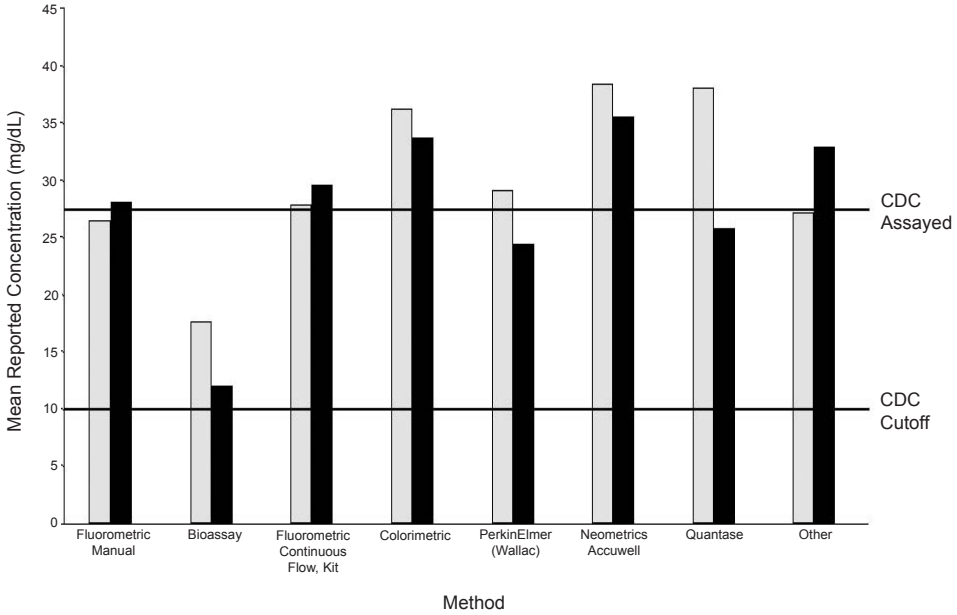
	Quarter 1	Quarter 2
Specimens		
Enriched	23	24
CDC Assayed	21.9	21.7
Reported Mean	25.5	27.5
Specimens		
Enriched	22	28
CDC Assayed	20	25.6
Reported Mean	22.8	30.5
Specimens		
Enriched	5	5
CDC Assayed	2.3	2.3
Reported Mean	5.7	4.3
Specimens		
Enriched	0	0
CDC Assayed	1.2	1.2
Reported Mean	2.1	2
Specimens		
Enriched	5	5
CDC Assayed	3.8	2.3
Reported Mean	5.7	5

Figure 15. Total Galactose Single-Specimen Method Comparison
No Within Run Data Available
Presumptive Clinical Assessment = Not Evaluated



	Quarter 3	Quarter 4
Specimens		
Enriched	0	25
CDC Assayed	0.1	27.4
Reported Mean	2	28.1
Specimens		
Enriched	13	0
CDC Assayed	11.8	0.1
Reported Mean	12.1	2.2
Specimens		
Enriched	23	23
CDC Assayed	26.6	26.6
Reported Mean	27.5	27.0
Specimens		
Enriched	0	5
CDC Assayed	0.3	6.2
Reported Mean	2.3	7.1
Specimens		
Enriched	25	0
CDC Assayed	27.5	0.7
Reported Mean	29.2	2.1

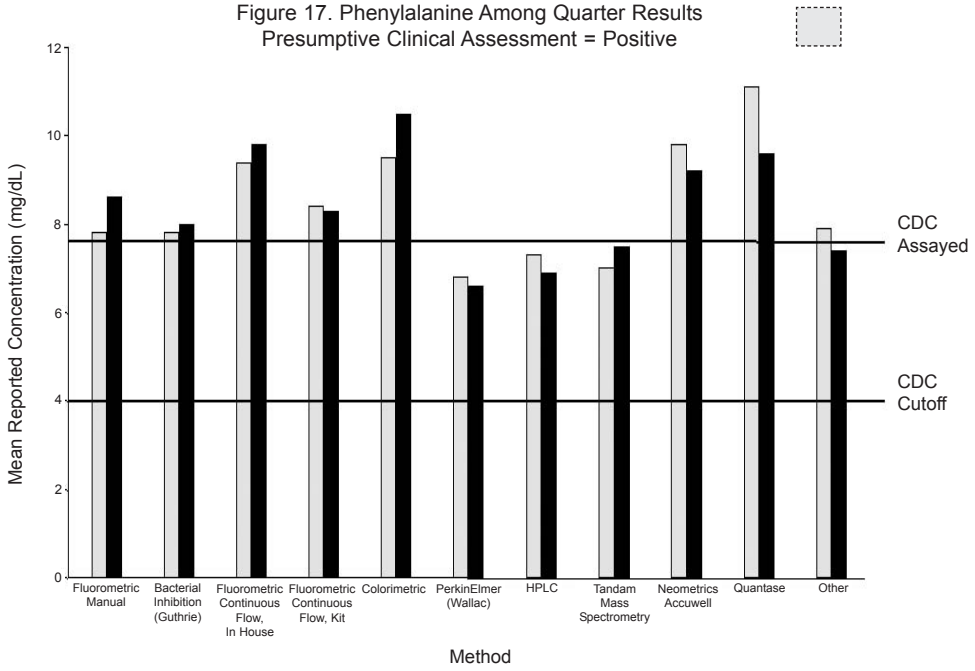
Figure 16. Total Galactose Among Quarter Results
Presumptive Clinical Assessment = Positive



FIGURES 17-18. Reproducibility of Results by Different Methods - Phenylalanine

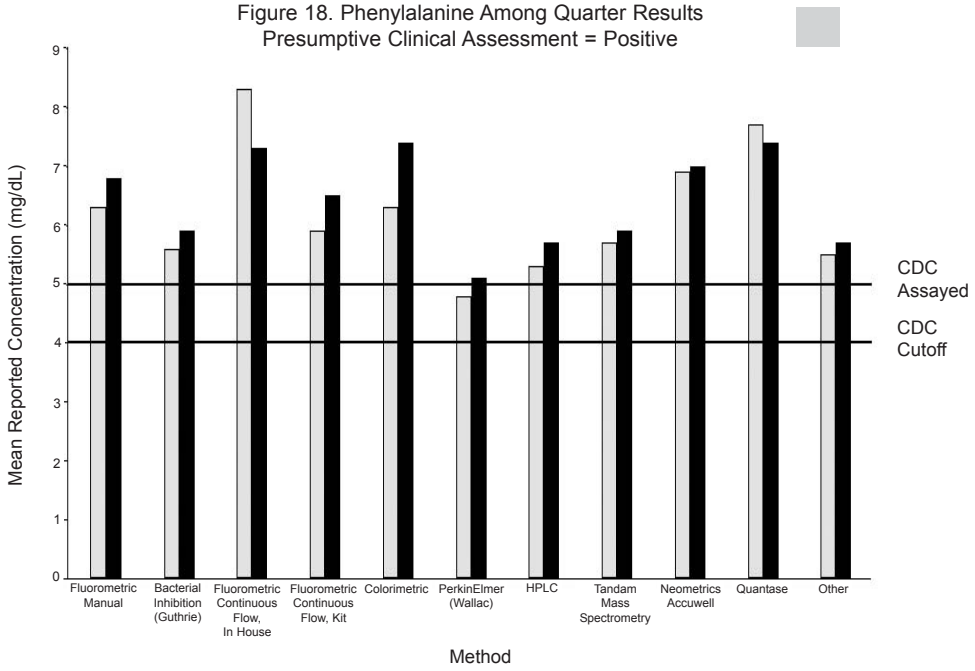
	Quarter 1	Quarter 2
Specimens		
Enriched	0	6
CDC Assayed	1.2	8.4
Reported Mean	1.3	7.8
Specimens		
Enriched	3	0
CDC Assayed	5	0.9
Reported Mean	4.6	1.2
Specimens		
Enriched	0	0
CDC Assayed	0.9	0.9
Reported Mean	1.3	1.2
Specimens		
Enriched	5.5	5.5
CDC Assayed	7.6	7.6
Reported Mean	7.9	7.9
Specimens		
Enriched	6	0
CDC Assayed	7.3	0.9
Reported Mean	7.7	1.3

Figure 17. Phenylalanine Among Quarter Results
Presumptive Clinical Assessment = Positive



	Quarter 3	Quarter 4
Specimens		
Enriched	0	5
CDC Assayed	0.6	5
Reported Mean	0.8	6.1
Specimens		
Enriched	0	0
CDC Assayed	1.1	0.6
Reported Mean	1.3	0.9
Specimens		
Enriched	0	0
CDC Assayed	0.3	0.3
Reported Mean	0.5	0.6
Specimens		
Enriched	5.5	2.5
CDC Assayed	5.2	3.3
Reported Mean	5.9	4.1
Specimens		
Enriched	5	6
CDC Assayed	5	5.7
Reported Mean	5.8	7.4

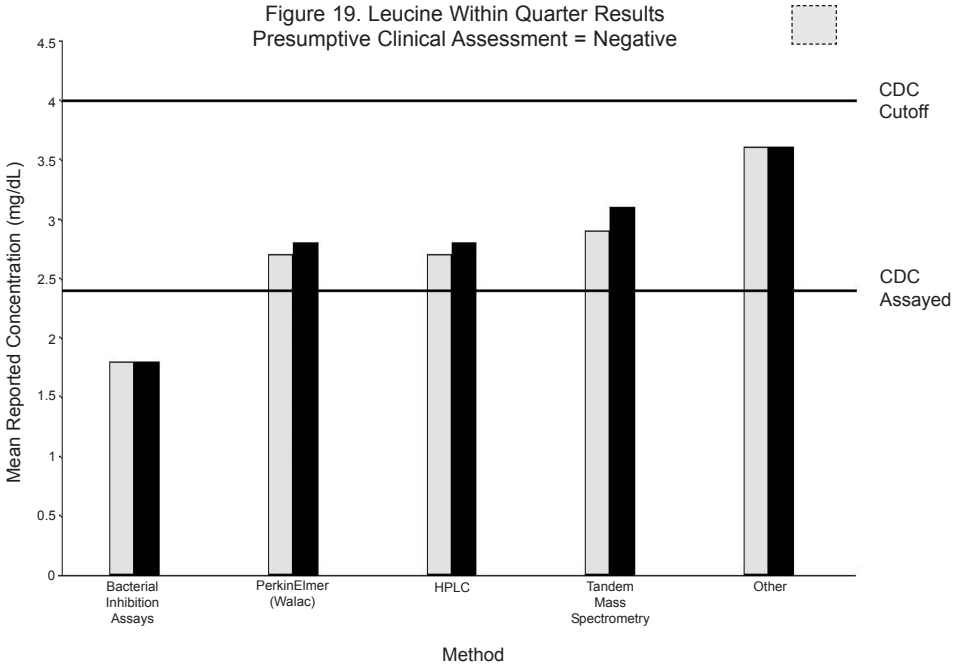
Figure 18. Phenylalanine Among Quarter Results
Presumptive Clinical Assessment = Positive



FIGURES 19-20. Reproducibility of Results by Different Methods - Leucine

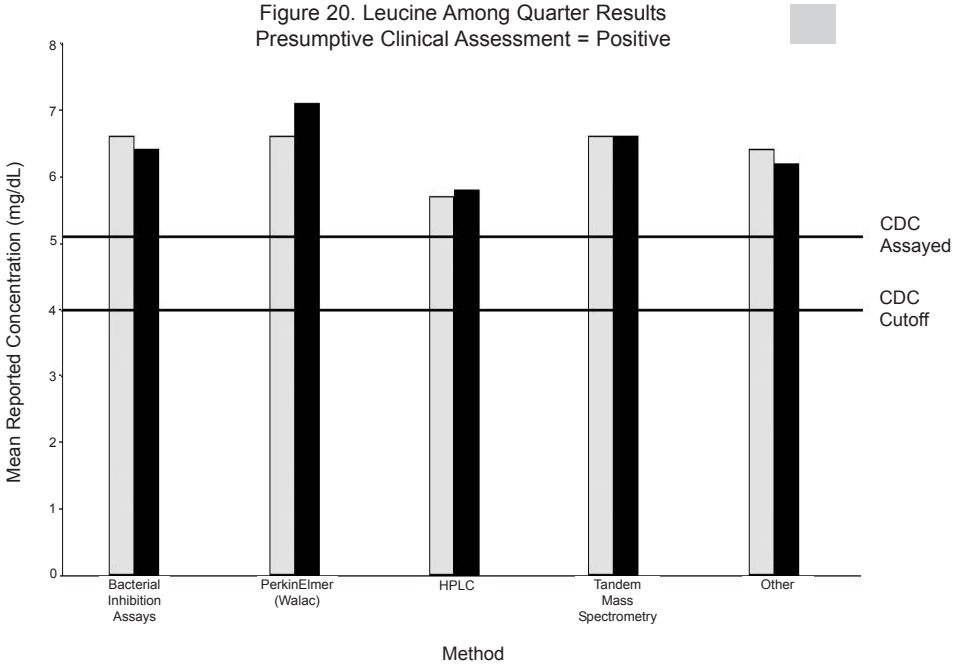
	Quarter 1	Quarter 2
Specimens		
Enriched	0	6
CDC Assayed	2.6	8.7
Reported Mean	2.7	7.3
Specimens		
Enriched	5.5	0
CDC Assayed	7.8	2
Reported Mean	6.7	2.4
Specimens		
Enriched	0	0
CDC Assayed	2.4	2.4
Reported Mean	2.7	2.6
Specimens		
Enriched	5.5	5.5
CDC Assayed	8	8
Reported Mean	8.4	8.7
Specimens		
Enriched	6.5	0
CDC Assayed	7.6	2.4
Reported Mean	7.9	2.7

Figure 19. Leucine Within Quarter Results
Presumptive Clinical Assessment = Negative



	Quarter 3	Quarter 4
Specimens		
Enriched	3	5
CDC Assayed	4.7	5.1
Reported Mean	4.7	6.4
Specimens		
Enriched	0	3
CDC Assayed	2.5	4.7
Reported Mean	2.8	4.7
Specimens		
Enriched	0	0
CDC Assayed	1.2	1.2
Reported Mean	1.2	1.3
Specimens		
Enriched	0	5
CDC Assayed	1.2	6.7
Reported Mean	1.2	7.3
Specimens		
Enriched	5	0
CDC Assayed	5.1	2.9
Reported Mean	6.5	2.5

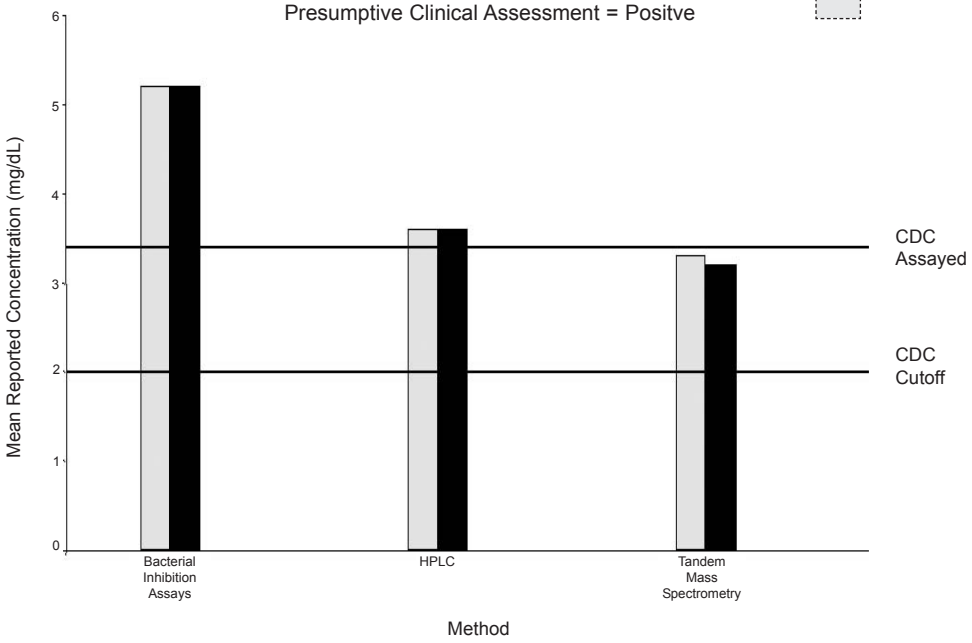
Figure 20. Leucine Among Quarter Results
Presumptive Clinical Assessment = Positive



FIGURES 21-22. Reproducibility of Results by Different Methods - Methionine

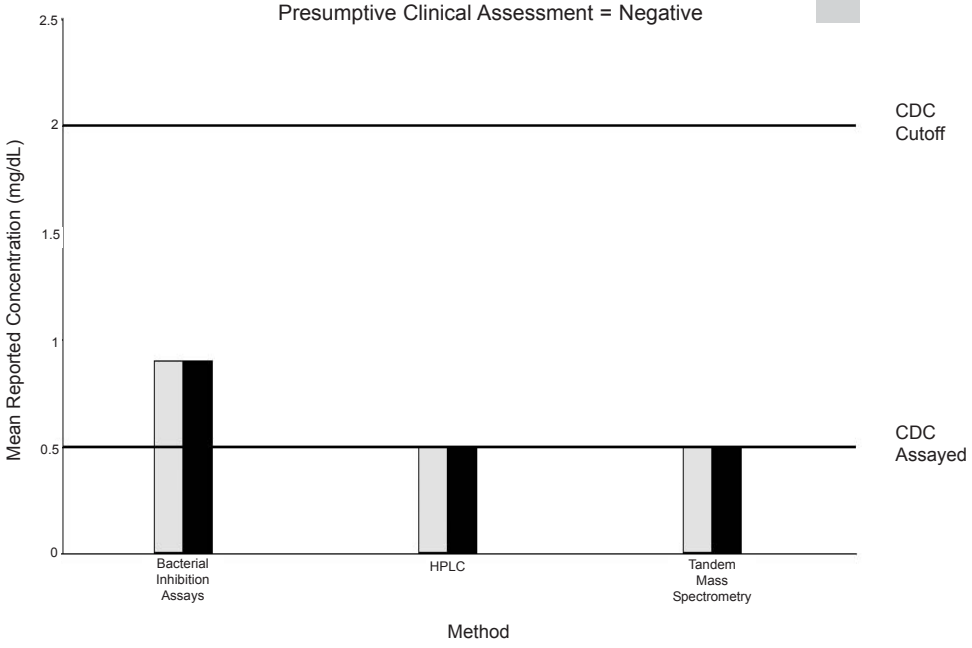
	Quarter 1	Quarter 2
Specimens		
Enriched	3	1
CDC Assayed	3.6	1.6
Reported Mean	3.2	1.3
Specimens		
Enriched	6	2.5
CDC Assayed	7.5	2.5
Reported Mean	6.1	2.5
Specimens		
Enriched	3.5	3.5
CDC Assayed	3.4	3.4
Reported Mean	3.8	3.7
Specimens		
Enriched	0	0
CDC Assayed	0.5	0.5
Reported Mean	0.6	0.5
Specimens		
Enriched	0	3.5
CDC Assayed	0.3	3.4
Reported Mean	0.4	3.6

Figure 21. Methionine Within Quarter Results
Presumptive Clinical Assessment = Positve



	Quarter 3	Quarter 4
Specimens		
Enriched	0	0
CDC Assayed	0	0.3
Reported Mean	0.3	0.3
Specimens		
Enriched	1	0
CDC Assayed	1.2	0
Reported Mean	1	0.3
Specimens		
Enriched	2.5	2.5
CDC Assayed	2.2	2.2
Reported Mean	2	2.6
Specimens		
Enriched	3	3
CDC Assayed	2.7	3
Reported Mean	2.7	3.4
Specimens		
Enriched	0	0
CDC Assayed	0.3	0.4
Reported Mean	0.3	0.5

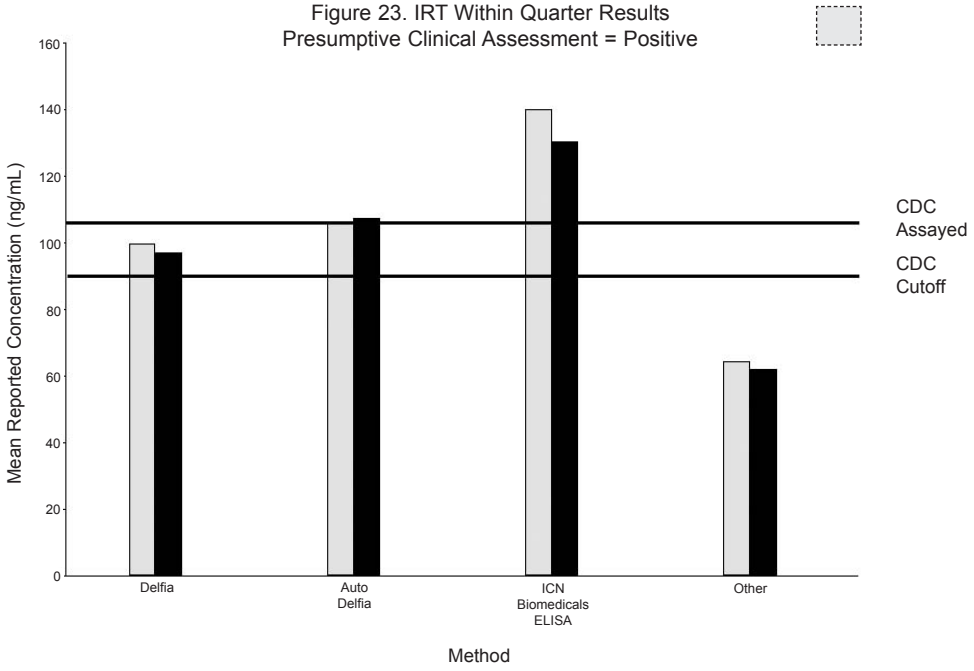
Figure 22. Methionine Among Quarter Results
Presumptive Clinical Assessment = Negative



FIGURES 23-24. Reproducibility of Results by Different Methods - Immunoreactive Trypsinogen (IRT)

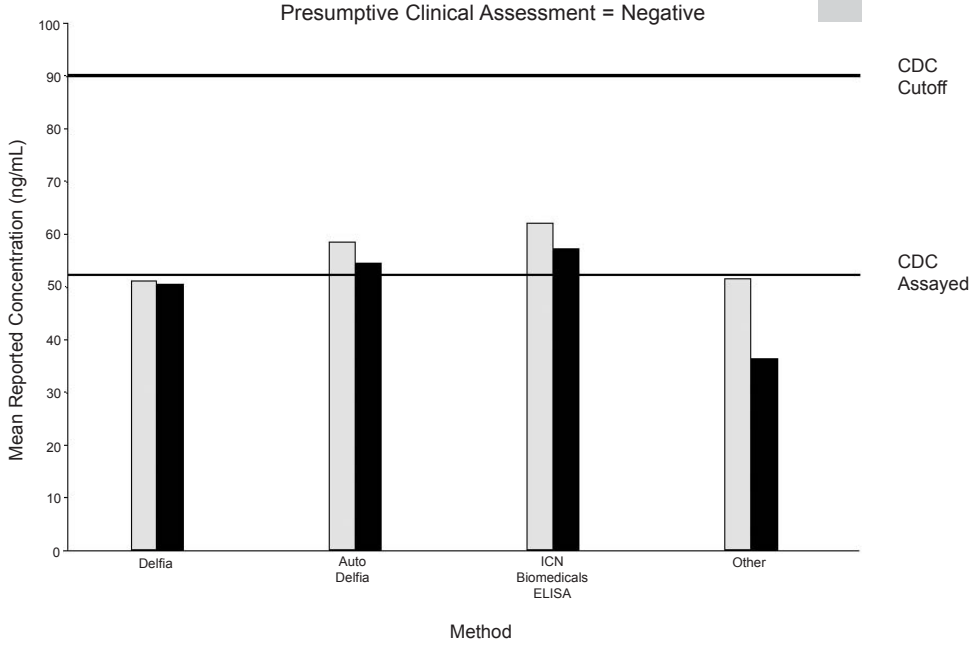
	Quarter 3
Specimens	
Enriched	80
CDC Assayed	52.3
Reported Mean	55
Specimens	
Enriched	0
CDC Assayed	15.9
Reported Mean	14.8
Specimens	
Enriched	200
CDC Assayed	105.9
Reported Mean	107.4
Specimens	
Enriched	400
CDC Assayed	177.8
Reported Mean	176.9
Specimens	
Enriched	0
CDC Assayed	15.9
Reported Mean	14.6

Figure 23. IRT Within Quarter Results
Presumptive Clinical Assessment = Positive



	Quarter 4
Specimens	
Enriched	400
CDC Assayed	177.8
Reported Mean	174.7
Specimens	
Enriched	0
CDC Assayed	15.9
Reported Mean	14.4
Specimens	
Enriched	200
CDC Assayed	105.9
Reported Mean	102.8
Specimens	
Enriched	80
CDC Assayed	52.3
Reported Mean	51.5
Specimens	
Enriched	200
CDC Assayed	105.9
Reported Mean	102

Figure 24. IRT Among Quarter Results
Presumptive Clinical Assessment = Negative



tions and thus rigorously tested the ability of laboratories to make the expected cutoff decision. Most specimens near the mean cutoff value are distributed as not-evaluated specimens and are not included in Table 1. Participants' data for these specimens are used to examine the relative analytical performance of the assays. Table 2 shows the performance errors for hemoglobinopathies. The percentage of errors for qualitative assessments for sickle cell disease and other hemoglobinopathies ranged from 0% to 0.8% for the error categories, with 65 of 68 laboratories correctly classifying all specimens. The classification errors are essentially the same for phenotype and clinical assessments within the domestic and foreign laboratory groups. Table 3 shows the most common reasons for false-negative errors reported by domestic participants upon follow-up by NSQAP. Low quantitative values are the most frequent explanation. These low results are unique to the false-negative reports and are different from 90% of the participants' reported values.

Generally, slope values substantially different from 1.0 indicate that a method has an analytic bias.

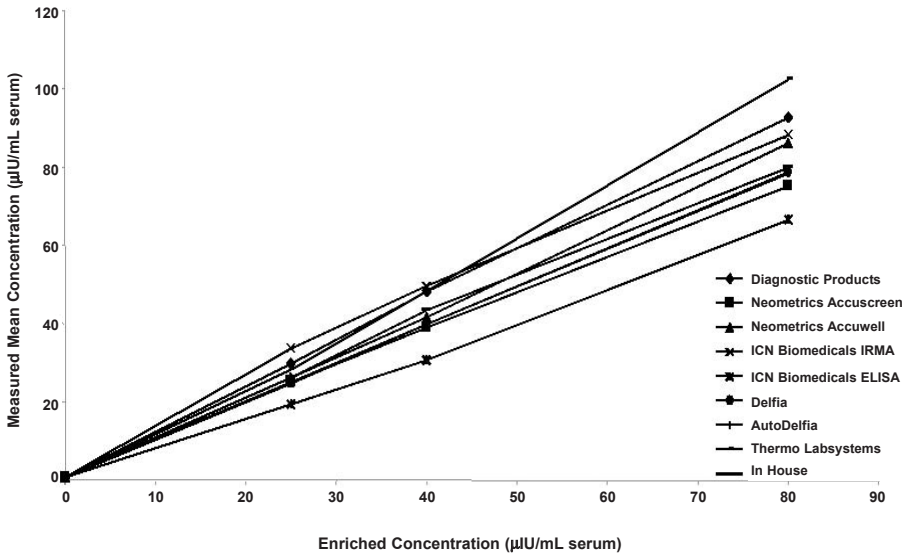
QUALITY CONTROL

For QC shipments of T_4, TSH, 17-OHP, Gal, Phe, Leu, Met, Tyr, Val, and Cit, each lot contained a different analyte concentration. To ensure that a laboratory received representative sheets of the production batch, we used a randomizing system to select the set of sheets from the production batch for each laboratory. The QC materials were distributed semiannually and included the blood-spot sheets, instructions for storage and analysis, and data-report forms. Data from five analytic runs of each lot and shipment were compiled in the midyear and annual summary reports that were distributed to each participant. Intervals between runs were not the same for all laboratories because each participant's reported data cover a different time span.

Figure 25 shows a performance comparison of different methods for measuring TSH from one set of QC materials distributed in 2002. The Y-intercept, which was not measured by participants, is the mean endogenous TSH level. Slope and Y-intercept data presented in this figure are shown in Table 4b (Lots 211-213). One method has a slope of 1.0 with a Y-intercept of 1.1 µIU/mL and falls in the middle of the cluster of lines. The reported QC data are summarized in Tables 4a-4j, which show the analyte by series of QC lots, the number of measurements (N), the mean values, and the standard deviations (SD) by kit or analytic method. In addition, we used a weighted linear regression analysis to examine the comparability by method of reported versus enriched concentrations. Linear regressions (Y-intercept and slope) were calculated by method for all analytic values within an analyte QC series. Values outside the 99% confidence limits (outliers) were excluded from the calculations.

Tables 4a-4j, which summarize reported QC results, provide data about method-related differences in analytic recoveries and method bias. Because we prepared each QC lot series from a single batch of hematocrit-adjusted, nonenriched blood, the endogenous concentration was the same for all specimens in a lot series. We calculated the within-laboratory SD component of the total SD and used the reported QC data from multiple analytic runs for

FIGURE 25. Comparison of Different Methods for Detecting Thyroid-Stimulating Hormone in Dried-Blood Spots (Lots 211-213)



NOTE: Y-intercept = CDC measured endogenous level

regression analyses. We calculated the Y-intercept and slope in each table using all analyte concentrations within a lot series (e.g., lots 211, 212, and 213). Because only three or four concentrations of QC materials are available for each analyte, a bias error in any one pool can markedly influence the slope and intercept. The Y-intercept provides one measure of the endogenous concentration level for an analyte. For Phe, Leu, Met, Tyr, Val, and Cit, participants also measured the endogenous concentrations by analyzing the nonenriched QC lots; the Y-intercepts and measured endogenous levels for these analytes were similar for most methods. Ideally, the slope should be 1.0, and most slopes were close to this value, ranging from 0.8 to 1.2. One of the Gal methods shows a lower-than-expected slope of 0.5 and several other Gal methods yield slopes of 1.4. The slope for one method for valine and citrulline was 0.6 and 0.7, respectively. These slope deviations may be related to analytic ranges for calibration curves or to low recoveries for one specimen in a three- or four-specimen QC set. Because the endogenous concentration was the same for all QC lots within a series, it should not affect the slope of the regression line among methods. Generally, slope values substantially different from 1.0 indicate that a method has an analytic bias.

REFERENCES

1. Hannon WH, Boyle J, Davin B, Marsden A, McCabe ERB, Schwartz M, et al. Blood collection on filter paper for neonatal screening programs. Third edition, approved standard. Wayne (PA): National Committee for Clinical Laboratory Standards; 1997 NCCLS Document LA4-A3.

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Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services or the Association of Public Health Laboratories.

TABLE 4a. 2002 Quality Control Data
Summaries of Statistical Analyses

THYROXINE (µg T_4/dL serum)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 001 - Enriched 2 µg/dL serum						
Diagnostic Products	28	2.7	0.7	0.7	0.7	1.0
ICN Biomedicals RIA	79	2.6	0.4	0.6	1.0	0.9
Neometrics Accuscreen	29	2.7	0.8	0.9	0.4	1.1
Neometrics Neocoat	58	2.5	0.5	0.6	0.8	0.9
Neometrics Accuwell	127	2.6	0.6	0.8	0.7	1.0
Delfia	163	2.3	0.5	1.2	0.7	0.8
AutoDelfia	368	2.1	0.7	0.8	0.4	0.8
Other	60	2.6	0.5	0.6	0.8	1.0
Lot 002 - Enriched 5.5 µg/dL serum						
Diagnostic Products	30	6.4	1.1	1.1	0.7	1.0
ICN Biomedicals RIA	100	6.0	0.7	0.7	1.0	0.9
Neometrics Accuscreen	30	6.0	0.8	1.4	0.4	1.1
Neometrics Neocoat	59	6.4	0.8	0.9	0.8	0.9
Neometrics Accuwell	125	6.0	0.9	1.0	0.7	1.0
Delfia	164	5.5	0.9	2.5	0.7	0.8
AutoDelfia	367	5.3	1.0	1.7	0.4	0.8
Other	60	6.5	0.8	1.0	0.8	1.0
Lot 003 - Enriched 8 µg/dL serum						
Diagnostic Products	30	8.9	1.4	1.5	0.7	1.0
ICN Biomedicals RIA	100	7.8	0.8	0.9	1.0	0.9
Neometrics Accuscreen	29	9.2	1.8	1.8	0.4	1.1
Neometrics Neocoat	60	8.1	1.0	1.2	0.8	0.9
Neometrics Accuwell	127	8.4	1.1	1.1	0.7	1.0
Delfia	159	7.2	1.3	3.4	0.7	0.8
AutoDelfia	370	7.1	4.8	6.3	0.4	0.8
Other	59	8.4	1.3	1.9	0.8	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

THYROXINE (µg T_4/dL serum)

- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 101 - Enriched 2 µg/dL serum						
Diagnostic Products	10	2.9	0.3	0.3	0.9	1.0
ICN Biomedicals RIA	40	2.4	0.3	0.6	0.9	0.8
Neometrics Accuscreen	10	3.6	0.8	0.8	1.7	0.9
Neometrics Neocoat	40	2.2	0.4	0.6	0.4	0.9
Neometrics Accuwell	79	2.8	0.6	0.8	0.9	0.9
Delfia	76	2.0	0.5	1.1	0.2	0.9
AutoDelfia	176	2.0	0.4	0.4	0.5	0.8
Other	19	2.4	0.5	0.5	0.6	1.0
Lot 102 - Enriched 5.5 µg/dL serum						
Diagnostic Products	10	6.6	0.5	0.5	0.9	1.0
ICN Biomedicals RIA	48	5.6	0.5	0.6	0.9	0.8
Neometrics Accuscreen	10	6.0	0.7	0.7	1.7	0.9
Neometrics Neocoat	40	5.6	0.9	1.1	0.4	0.9
Neometrics Accuwell	78	6.2	0.8	1.0	0.9	0.9
Delfia	77	5.3	0.9	1.9	0.2	0.9
AutoDelfia	176	5.1	0.6	0.7	0.5	0.8
Other	20	6.2	0.9	0.9	0.6	1.0
Lot 103 - Enriched 8 µg/dL serum						
Diagnostic Products	10	9.0	0.9	0.9	0.9	1.0
ICN Biomedicals RIA	49	7.3	0.9	1.0	0.9	0.8
Neometrics Accuscreen	10	8.8	1.3	1.3	1.7	0.9
Neometrics Neocoat	39	7.7	0.8	1.0	0.4	0.9
Neometrics Accuwell	79	8.5	1.0	1.4	0.9	0.9
Delfia	68	7.4	2.6	4.5	0.2	0.9
AutoDelfia	177	6.9	0.8	0.9	0.5	0.8
Other	20	8.1	0.9	1.1	0.6	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4b. 2002 Quality Control Data
Summaries of Statistical Analyses

THYROID-STIMULATING HORMONE (µIU/mL serum)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 111 - Enriched 25 µIU/mL serum						
Diagnostic Products	77	29.3	6.6	9.2	-1.7	1.2
Neometrics Accuscreen	60	24.3	3.5	4.0	1.4	0.9
Neometrics Accuwell	79	22.7	3.4	3.8	-0.6	1.0
ICN Biomedicals IRMA	144	31.9	3.8	10.4	4.1	1.1
ICN Biomedicals ELISA	120	21.2	2.3	4.1	-0.7	0.9
Delfia	745	24.3	4.3	6.7	-0.1	1.0
AutoDelfia	733	24.0	2.7	3.9	0.0	1.0
Thermo Labsystems	50	24.6	2.9	9.1	-1.5	1.0
In House	146	25.0	3.0	4.7	-0.1	1.0
Other	565	26.8	6.1	9.4	2.0	1.0
Lot 112 - Enriched 40 µIU/mL serum						
Diagnostic Products	74	45.4	6.6	13.4	-1.7	1.2
Neometrics Accuscreen	60	36.3	4.1	5.9	1.4	0.9
Neometrics Accuwell	78	39.8	5.5	5.6	-0.6	1.0
ICN Biomedicals IRMA	145	47.2	4.6	16.0	4.1	1.1
ICN Biomedicals ELISA	114	34.3	5.0	9.6	-0.7	0.9
Delfia	742	39.6	6.6	10.5	-0.1	1.0
AutoDelfia	731	39.0	4.6	6.7	0.0	1.0
Thermo Labsystems	50	40.0	4.7	10.9	-1.5	1.0
In House	149	41.6	6.5	7.7	-0.1	1.0
Other	560	42.3	9.0	14.4	2.0	1.0
Lot 113 - Enriched 80 µIU/mL serum						
Diagnostic Products	77	95.3	15.0	23.5	-1.7	1.2
Neometrics Accuscreen	59	73.0	9.5	12.3	1.4	0.9
Neometrics Accuwell	79	77.0	10.0	11.8	-0.6	1.0
ICN Biomedicals IRMA	148	91.7	10.1	25.1	4.1	1.1
ICN Biomedicals ELISA	120	69.5	5.3	9.7	-0.7	0.9
Delfia	733	78.7	11.0	17.5	-0.1	1.0
AutoDelfia	732	77.2	7.9	11.7	0.0	1.0
Thermo Labsystems	49	81.8	8.9	9.7	-1.5	1.0
In House	148	81.7	19.6	22.5	-0.1	1.0
Other	576	82.0	17.0	25.8	2.0	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

THYROID-STIMULATING HORMONE (µIU/mL serum)

- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 211 - Enriched 25 µIU/mL serum						
Diagnostic Products	39	29.8	3.1	3.2	2.0	1.1
Neometrics Accuscreen	30	25.1	4.4	4.4	2.5	0.9
Neometrics Accuwell	49	26.4	3.7	5.1	-1.5	1.1
ICN Biomedicals IRMA	77	33.8	3.3	5.5	9.6	1.0
ICN Biomedicals ELISA	129	19.4	2.7	4.1	-2.9	0.9
Delfia	417	24.7	3.7	6.6	0.3	1.0
AutoDelfia	356	25.1	2.3	3.3	1.1	1.0
Thermo Labsystems	30	28.5	3.8	9.8	-5.3	1.3
In House	100	26.3	3.1	4.5	3.3	1.0
Other	349	29.4	5.4	10.5	2.0	1.1
Lot 212 - Enriched 40 µIU/mL serum						
Diagnostic Products	39	48.2	3.3	3.8	2.0	1.1
Neometrics Accuscreen	30	39.1	5.3	5.3	2.5	0.9
Neometrics Accuwell	50	41.6	5.0	8.0	-1.5	1.1
ICN Biomedicals IRMA	77	49.6	4.6	8.4	9.6	1.0
ICN Biomedicals ELISA	129	30.7	3.7	5.7	-2.9	0.9
Delfia	421	39.9	6.2	11.1	0.3	1.0
AutoDelfia	351	40.0	4.4	5.4	1.1	1.0
Thermo Labsystems	30	48.3	7.0	10.6	-5.3	1.3
In House	100	43.5	4.5	7.8	3.3	1.0
Other	341	45.8	5.5	13.8	2.0	1.1
Lot 213 - Enriched 80 µIU/mL serum						
Diagnostic Products	39	92.6	5.5	8.3	2.0	1.1
Neometrics Accuscreen	29	75.2	8.3	8.3	2.5	0.9
Neometrics Accuwell	50	86.3	12.4	21.8	-1.5	1.1
ICN Biomedicals IRMA	78	88.4	6.2	16.7	9.6	1.0
ICN Biomedicals ELISA	130	66.6	6.2	9.6	-2.9	0.9
Delfia	423	78.9	9.6	18.8	0.3	1.0
AutoDelfia	356	78.5	7.9	9.3	1.1	1.0
Thermo Labsystems	30	102.5	9.6	21.4	-5.3	1.3
In House	97	80.1	12.1	16.2	3.3	1.0
Other	350	89.7	9.6	25.9	2.0	1.1

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4c. 2002 Quality Control Data
Summaries of Statistical Analyses

17 α-HYDROXYPROGESTERONE (ng 17-OHP/mL serum)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 151 - Enriched 25 ng/mL serum						
ICN Biomedicals RIA	39	26.6	2.1	2.1	5.2	0.9
Neometrics Accuscreen	59	26.7	2.4	2.7	7.3	0.8
Neometrics Accuwell	40	23.7	2.2	2.9	2.5	0.9
Delfia	258	26.2	3.6	4.9	2.3	1.0
AutoDelfia	448	27.7	3.2	4.0	2.3	1.0
Other	80	20.9	3.2	9.2	4.1	0.7
Lot 152 - Enriched 50 ng/mL serum						
ICN Biomedicals RIA	40	48.7	4.8	4.8	5.2	0.9
Neometrics Accuscreen	60	49.6	5.4	6.2	7.3	0.8
Neometrics Accuwell	39	47.5	3.7	7.9	2.5	0.9
Delfia	257	51.7	7.2	9.9	2.3	1.0
AutoDelfia	442	52.4	7.0	8.1	2.3	1.0
Other	80	40.0	5.8	18.4	4.1	0.7
Lot 153 - Enriched 100 ng/mL serum						
ICN Biomedicals RIA	40	91.6	6.4	6.7	5.2	0.9
Neometrics Accuscreen	60	88.3	11.9	14.7	7.3	0.8
Neometrics Accuwell	40	89.7	7.3	9.7	2.5	0.9
Delfia	254	99.6	13.4	21.1	2.3	1.0
AutoDelfia	437	103.1	13.0	17.7	2.3	1.0
Other	80	73.6	11.9	35.3	4.1	0.7

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

17 α-HYDROXYPROGESTERONE (ng 17-OHP/mL serum)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 657 - Enriched 25 ng/mL serum						
ICN Biomedicals RIA	20	25.1	2.2	3.2	4.6	0.8
Neometrics Accuscreen	20	26.3	2.0	2.0	10.5	0.7
Neometrics Accuwell	20	21.9	2.8	3.7	-4.2	1.0
Delfia	109	27.3	2.6	3.9	1.7	1.1
AutoDelfia	210	29.8	2.6	5.5	2.8	1.1
Other	20	11.7	0.9	0.9	-2.9	0.7
Lot 658 - Enriched 50 ng/mL serum						
ICN Biomedicals RIA	20	47.7	5.0	5.6	4.6	0.8
Neometrics Accuscreen	20	46.4	2.6	2.6	10.5	0.7
Neometrics Accuwell	19	46.3	7.2	7.2	-4.2	1.0
Delfia	109	55.4	5.7	7.2	1.7	1.1
AutoDelfia	210	57.6	5.5	10.6	2.8	1.1
Other	30	34.0	11.1	18.5	-2.9	0.7
Lot 659 - Enriched 100 ng/mL serum						
ICN Biomedicals RIA	20	88.7	7.4	9.5	4.6	0.8
Neometrics Accuscreen	20	77.9	6.3	6.3	10.5	0.7
Neometrics Accuwell	20	98.5	10.9	11.8	-4.2	1.0
Delfia	110	106.6	11.7	17.3	1.7	1.1
AutoDelfia	214	111.5	11.0	23.2	2.8	1.1
Other	30	64.9	20.8	26.2	-2.9	0.7

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4d. 2002 Quality Control Data
Summaries of Statistical Analyses

TOTAL GALACTOSE (mg Gal/dL whole blood)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 141 - Enriched 5 mg/dL whole blood						
Fluorometric Manual	116	5.5	0.9	1.9	0.1	1.0
Bioassay	30	5.4	0.9	1.0	4.1	0.5
Fluor Cont Flo, Kit	69	8.4	0.7	1.3	2.4	1.2
Colorimetric	50	7.2	1.1	3.0	0.0	1.4
PerkinElmer (Wallac)	118	6.4	1.5	1.7	2.1	1.0
Neometrics Accuwell	20	8.3	0.8	0.8	1.3	1.4
Quantase	49	7.0	0.9	0.9	-0.4	1.4
Other	50	5.9	0.8	2.6	1.1	1.0
Lot 142 - Enriched 10 mg/dL whole blood						
Fluorometric Manual	119	10.5	1.1	2.1	0.1	1.0
Bioassay	29	9.4	1.2	1.4	4.1	0.5
Fluor Cont Flo, Kit	70	14.2	0.8	1.9	2.4	1.2
Colorimetric	50	13.3	1.6	4.5	0.0	1.4
PerkinElmer (Wallac)	118	12.2	1.6	1.9	2.1	1.0
Neometrics Accuwell	20	14.5	1.2	1.3	1.3	1.4
Quantase	50	13.4	1.4	1.7	-0.4	1.4
Other	50	11.5	1.0	3.4	1.1	1.0
Lot 143 - Enriched 15 mg/dL whole blood						
Fluorometric Manual	119	15.3	1.2	2.7	0.1	1.0
Bioassay	30	14.3	1.3	2.3	4.1	0.5
Fluor Cont Flo, Kit	68	20.1	1.4	2.4	2.4	1.2
Colorimetric	50	20.7	1.6	6.3	0.0	1.4
PerkinElmer (Wallac)	120	17.3	1.7	2.2	2.1	1.0
Neometrics Accuwell	20	21.9	2.2	2.5	1.3	1.4
Quantase	50	20.4	1.8	2.8	-0.4	1.4
Other	50	17.4	1.6	4.2	1.1	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TOTAL GALACTOSE (mg Gal/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 144 - Enriched 30 mg/dL whole blood						
Fluorometric Manual	116	31.3	2.3	4.4	0.1	1.0
Bioassay	20	18.6	2.1	2.8	4.1	0.5
Fluor Cont Flo, Kit	70	37.9	3.0	5.6	2.4	1.2
Colorimetric	50	41.3	4.5	14.9	0.0	1.4
PerkinElmer (Wallac)	119	31.2	2.8	3.2	2.1	1.0
Neometrics Accuwell	20	42.2	3.1	3.2	1.3	1.4
Quantase	50	41.8	4.6	10.5	-0.4	1.4
Other	49	32.1	5.3	9.9	1.1	1.0
Lot 221 - Enriched 5 mg/dL whole blood						
Fluorometric Manual	227	5.3	1.0	2.0	1.0	1.0
Bioassay	40	4.0	0.8	1.2	1.7	0.6
Fluor Cont Flo, Kit	138	6.7	0.6	0.8	2.3	1.0
Colorimetric	110	6.7	1.1	2.7	0.5	1.3
PerkinElmer (Wallac)	234	8.2	1.3	1.5	4.6	0.9
Neometrics Accuwell	79	7.7	0.9	0.9	2.0	1.3
Quantase	99	5.5	1.0	1.5	1.1	1.1
Other	100	5.9	0.7	1.8	1.9	1.0
Lot 222 - Enriched 10 mg/dL whole blood						
Fluorometric Manual	222	10.4	1.2	2.2	1.0	1.0
Bioassay	40	7.6	0.8	0.9	1.7	0.6
Fluor Cont Flo, Kit	138	12.2	1.2	1.5	2.3	1.0
Colorimetric	110	12.3	1.7	3.5	0.5	1.3
PerkinElmer (Wallac)	236	12.8	1.7	1.8	4.6	0.9
Neometrics Accuwell	80	13.8	1.7	2.0	2.0	1.3
Quantase	99	10.8	1.4	2.5	1.1	1.1
Other	99	11.5	0.9	2.5	1.9	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TOTAL GALACTOSE (mg Gal/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 223 - Enriched 15 mg/dL whole blood						
Fluorometric Manual	226	16.8	1.8	2.8	1.0	1.0
Bioassay	40	12.1	2.0	2.7	1.7	0.6
Fluor Cont Flo, Kit	134	19.4	1.3	2.1	2.3	1.0
Colorimetric	110	21.1	2.3	5.4	0.5	1.3
PerkinElmer (Wallac)	236	19.1	2.1	2.2	4.6	0.9
Neometrics Accuwell	79	23.4	2.6	2.7	2.0	1.3
Quantase	98	19.5	2.4	4.0	1.1	1.1
Other	97	20.1	1.7	4.3	1.9	1.0
Lot 224 - Enriched 30 mg/dL whole blood						
Fluorometric Manual	224	29.6	2.6	3.5	1.0	1.0
Bioassay	29	19.0	2.1	3.0	1.7	0.6
Fluor Cont Flo, Kit	138	32.5	2.5	3.3	2.3	1.0
Colorimetric	100	38.2	5.0	8.2	0.5	1.3
PerkinElmer (Wallac)	234	29.6	3.1	3.3	4.6	0.9
Neometrics Accuwell	77	39.5	4.8	5.5	2.0	1.3
Quantase	100	32.0	4.1	9.3	1.1	1.1
Other	97	31.7	2.8	6.9	1.9	1.0
Lot 241 - Enriched 5 mg/dL whole blood						
Fluorometric Manual	113	5.9	0.7	2.2	1.2	1.0
Bioassay	20	3.0	0.2	1.4	0.3	0.6
Fluor Cont Flo, Kit	70	7.4	0.7	1.1	2.1	1.1
Colorimetric	60	7.6	0.5	1.7	1.6	1.2
PerkinElmer (Wallac)	117	7.8	1.3	1.8	4.3	0.8
Neometrics Accuwell	39	8.4	0.8	1.2	2.1	1.4
Quantase	50	6.1	1.0	1.7	3.0	0.9
Other	40	6.9	0.7	1.7	2.1	1.1

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TOTAL GALACTOSE (mg Gal/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 242 - Enriched 10 mg/dL whole blood						
Fluorometric Manual	118	10.6	1.0	2.0	1.2	1.0
Bioassay	20	6.8	0.8	0.8	0.3	0.6
Fluor Cont Flo, Kit	69	12.7	1.0	1.5	2.1	1.1
Colorimetric	60	13.6	1.2	2.5	1.6	1.2
PerkinElmer (Wallac)	120	12.9	1.5	2.0	4.3	0.8
Neometrics Accuwell	40	15.8	1.2	1.9	2.1	1.4
Quantase	50	12.4	1.2	3.3	3.0	0.9
Other	40	13.5	1.3	2.7	2.1	1.1
Lot 243 - Enriched 15 mg/dL whole blood						
Fluorometric Manual	117	15.6	1.5	2.1	1.2	1.0
Bioassay	20	9.5	0.8	1.5	0.3	0.6
Fluor Cont Flo, Kit	68	18.3	1.1	2.5	2.1	1.1
Colorimetric	60	20.5	1.6	3.2	1.6	1.2
PerkinElmer (Wallac)	120	17.3	1.8	2.8	4.3	0.8
Neometrics Accuwell	40	23.0	1.8	2.4	2.1	1.4
Quantase	50	17.8	2.1	4.6	3.0	0.9
Other	40	19.4	1.6	3.5	2.1	1.1
Lot 244 - Enriched 30 mg/dL whole blood						
Fluorometric Manual	119	29.7	2.3	3.6	1.2	1.0
Bioassay	20	18.4	1.7	1.7	0.3	0.6
Fluor Cont Flo, Kit	69	34.2	2.0	4.3	2.1	1.1
Colorimetric	58	38.2	4.7	7.0	1.6	1.2
PerkinElmer (Wallac)	119	28.9	2.8	4.1	4.3	0.8
Neometrics Accuwell	40	42.5	2.9	6.2	2.1	1.4
Quantase	49	28.7	4.6	6.9	3.0	0.9
Other	40	34.8	2.9	5.3	2.1	1.1

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4e. 2002 Quality Control Data
Summaries of Statistical Analyses

PHENYLALANINE (mg Phe/dL whole blood)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 141 - Nonenriched 0 mg/dL whole blood						
Fluorometric Manual	40	1.6	0.5	0.8	1.8	1.2
Bacterial Inhibition	158	1.5	0.5	0.8	1.6	1.0
Fluor Cont Flo, In-house	10	1.8	0.1	0.1	1.8	1.3
Fluor Cont Flo, Kit	129	1.6	0.2	0.6	1.6	1.2
Colorimetric	98	1.9	0.3	0.4	1.9	1.3
PerkinElmer (Wallac)	274	1.3	0.3	0.4	1.2	1.0
HPLC	79	1.2	0.1	0.2	1.3	1.1
Tandem Mass Spec	126	1.3	0.2	0.3	1.3	1.0
Neometrics Accuwell	58	1.9	0.6	0.6	2.0	1.3
Quantase	99	1.8	0.4	0.7	2.1	1.3
Other	80	1.7	0.3	0.6	1.7	1.0
Lot 142 - Enriched 3 mg/dL whole blood						
Fluorometric Manual	40	5.6	0.7	1.5	1.8	1.2
Bacterial Inhibition	175	4.8	0.8	1.2	1.6	1.0
Fluor Cont Flo, In-house	10	5.8	0.6	0.6	1.8	1.3
Fluor Cont Flo, Kit	127	5.1	0.4	1.0	1.6	1.2
Colorimetric	99	5.8	0.5	0.6	1.9	1.3
PerkinElmer (Wallac)	273	4.2	0.5	0.6	1.2	1.0
HPLC	79	4.4	0.4	0.5	1.3	1.1
Tandem Mass Spec	129	4.4	0.4	0.7	1.3	1.0
Neometrics Accuwell	59	5.7	0.6	0.9	2.0	1.3
Quantase	100	6.1	0.6	1.5	2.1	1.3
Other	78	4.8	0.7	1.1	1.7	1.0
Lot 143 - Enriched 7 mg/dL whole blood						
Fluorometric Manual	40	10.3	0.9	2.6	1.8	1.2
Bacterial Inhibition	177	9.0	1.2	1.8	1.6	1.0
Fluor Cont Flo, In-house	10	10.8	1.0	1.0	1.8	1.3
Fluor Cont Flo, Kit	126	9.7	0.8	1.7	1.6	1.2
Colorimetric	99	11.4	0.8	1.4	1.9	1.3
PerkinElmer (Wallac)	264	8.1	0.8	1.1	1.2	1.0
HPLC	80	9.0	0.7	1.0	1.3	1.1
Tandem Mass Spec	128	8.8	0.9	1.5	1.3	1.0
Neometrics Accuwell	59	11.0	1.1	1.8	2.0	1.3
Quantase	100	11.7	0.8	2.5	2.1	1.3
Other	79	8.9	0.8	1.8	1.7	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

PHENYLALANINE (mg Phe/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 144 - Enriched 11 mg/dL whole blood						
Fluorometric Manual	40	14.7	1.5	3.7	1.8	1.2
Bacterial Inhibition	178	13.0	1.9	3.0	1.6	1.0
Fluor Cont Flo, In-house	10	16.3	0.9	0.9	1.8	1.3
Fluor Cont Flo, Kit	124	14.3	1.2	2.7	1.6	1.2
Colorimetric	90	16.3	1.3	2.2	1.9	1.3
PerkinElmer (Wallac)	273	12.2	1.1	1.8	1.2	1.0
HPLC	80	13.0	1.0	1.2	1.3	1.1
Tandem Mass Spec	129	12.7	1.2	2.2	1.3	1.0
Neometrics Accuwell	60	15.6	1.3	2.4	2.0	1.3
Quantase	100	16.1	1.2	3.1	2.1	1.3
Other	78	13.0	1.2	2.6	1.7	1.0
Lot 221 - Nonenriched 0 mg/dL whole blood						
Fluorometric Manual	119	1.5	0.4	0.7	1.5	1.0
Bacterial Inhibition	306	1.4	0.3	0.6	1.4	1.0
Fluor Cont Flo, In-house	48	1.7	0.2	0.4	1.7	1.2
Fluor Cont Flo, Kit	225	1.6	0.2	0.5	1.7	1.0
Colorimetric	184	1.4	0.3	0.5	1.3	1.2
PerkinElmer (Wallac)	543	1.2	0.3	0.3	1.2	0.9
HPLC	166	1.2	0.2	0.2	1.1	1.0
Tandem Mass Spec	295	1.3	0.3	0.4	1.3	0.9
Neometrics Accuwell	147	1.5	0.5	0.6	1.4	1.2
Quantase	233	1.4	0.4	0.8	1.4	1.1
Other	157	1.5	0.3	0.6	1.4	0.9
Lot 222 - Enriched 3 mg/dL whole blood						
Fluorometric Manual	117	4.4	0.7	1.1	1.5	1.0
Bacterial Inhibition	329	4.3	0.7	1.0	1.4	1.0
Fluor Cont Flo, In-house	50	5.2	0.4	0.8	1.7	1.2
Fluor Cont Flo, Kit	227	4.9	0.7	1.0	1.7	1.0
Colorimetric	196	4.8	0.7	1.0	1.3	1.2
PerkinElmer (Wallac)	551	3.8	0.6	0.7	1.2	0.9
HPLC	180	4.0	0.3	0.5	1.1	1.0
Tandem Mass Spec	297	4.1	0.4	0.8	1.3	0.9
Neometrics Accuwell	149	4.8	0.6	0.8	1.4	1.2
Quantase	239	4.6	0.6	1.3	1.4	1.1
Other	177	3.9	0.5	1.1	1.4	0.9

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

PHENYLALANINE (mg Phe/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 223 - Enriched 7 mg/dL whole blood						
Fluorometric Manual	113	8.5	1.2	1.9	1.5	1.0
Bacterial Inhibition	336	8.1	1.1	2.1	1.4	1.0
Fluor Cont Flo, In-house	50	10.0	0.6	1.5	1.7	1.2
Fluor Cont Flo, Kit	219	8.8	0.7	1.5	1.7	1.0
Colorimetric	198	9.3	1.0	1.6	1.3	1.2
PerkinElmer (Wallac)	555	7.3	0.9	1.0	1.2	0.9
HPLC	169	7.8	0.7	0.9	1.1	1.0
Tandem Mass Spec	297	7.9	0.8	1.5	1.3	0.9
Neometrics Accuwell	148	9.5	1.0	1.6	1.4	1.2
Quantase	238	9.1	1.2	1.9	1.4	1.1
Other	174	7.6	0.7	1.6	1.4	0.9
Lot 224 - Enriched 11 mg/dL whole blood						
Fluorometric Manual	115	12.5	1.5	2.4	1.5	1.0
Bacterial Inhibition	341	11.9	1.5	3.4	1.4	1.0
Fluor Cont Flo, In-house	50	14.5	1.1	2.4	1.7	1.2
Fluor Cont Flo, Kit	224	13.0	1.1	2.1	1.7	1.0
Colorimetric	178	14.2	1.4	2.6	1.3	1.2
PerkinElmer (Wallac)	539	10.9	1.1	1.5	1.2	0.9
HPLC	179	11.7	1.0	1.5	1.1	1.0
Tandem Mass Spec	290	11.7	1.1	2.4	1.3	0.9
Neometrics Accuwell	149	14.1	1.8	2.8	1.4	1.2
Quantase	238	13.3	1.8	2.9	1.4	1.1
Other	170	11.0	1.1	2.6	1.4	0.9
Lot 241 - Nonenriched 0 mg/dL whole blood						
Fluorometric Manual	80	1.3	0.2	0.5	1.0	1.1
Bacterial Inhibition	147	1.6	0.2	0.5	1.5	1.0
Fluor Cont Flo, In-house	40	1.7	0.1	0.5	1.6	1.3
Fluor Cont Flo, Kit	96	1.5	0.2	0.5	1.4	1.1
Colorimetric	99	1.5	0.3	0.3	1.5	1.2
PerkinElmer (Wallac)	291	1.0	0.2	0.3	1.0	0.9
HPLC	79	1.1	0.2	0.2	1.0	1.0
Tandem Mass Spec	187	1.1	0.1	0.3	1.1	1.0
Neometrics Accuwell	78	1.5	0.2	0.3	1.6	1.2
Quantase	106	1.5	0.4	0.7	1.6	1.2
Other	89	1.4	0.2	0.5	1.3	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

PHENYLALANINE (mg Phe/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 242 - Enriched 3 mg/dL whole blood						
Fluorometric Manual	80	4.1	0.5	0.9	1.0	1.1
Bacterial Inhibition	176	4.2	0.6	0.9	1.5	1.0
Fluor Cont Flo, In-house	40	5.3	0.4	0.7	1.6	1.3
Fluor Cont Flo, Kit	97	4.7	0.5	1.0	1.4	1.1
Colorimetric	99	5.1	0.5	0.7	1.5	1.2
PerkinElmer (Wallac)	292	3.6	0.5	0.6	1.0	0.9
HPLC	80	4.2	0.4	0.6	1.0	1.0
Tandem Mass Spec	188	4.0	0.6	0.9	1.1	1.0
Neometrics Accuwell	80	5.0	0.4	0.8	1.6	1.2
Quantase	107	5.2	0.8	1.3	1.6	1.2
Other	87	4.3	0.4	0.7	1.3	1.0
Lot 243 - Enriched 7 mg/dL whole blood						
Fluorometric Manual	78	8.4	1.0	1.4	1.0	1.1
Bacterial Inhibition	177	8.1	1.0	1.7	1.5	1.0
Fluor Cont Flo, In-house	40	10.5	0.6	1.9	1.6	1.3
Fluor Cont Flo, Kit	98	9.1	0.7	1.6	1.4	1.1
Colorimetric	100	10.2	0.7	1.7	1.5	1.2
PerkinElmer (Wallac)	295	7.3	0.8	0.9	1.0	0.9
HPLC	79	8.3	0.6	1.3	1.0	1.0
Tandem Mass Spec	185	7.9	1.0	1.8	1.1	1.0
Neometrics Accuwell	80	9.8	0.7	1.6	1.6	1.2
Quantase	109	10.2	0.9	2.1	1.6	1.2
Other	89	8.3	0.7	1.2	1.3	1.0
Lot 244 - Enriched 11 mg/dL whole blood						
Fluorometric Manual	78	13.1	1.4	2.0	1.0	1.1
Bacterial Inhibition	175	12.1	1.4	2.5	1.5	1.0
Fluor Cont Flo, In-house	40	15.8	1.3	3.1	1.6	1.3
Fluor Cont Flo, Kit	98	13.6	1.0	2.4	1.4	1.1
Colorimetric	98	15.1	1.1	2.6	1.5	1.2
PerkinElmer (Wallac)	286	11.1	1.1	1.3	1.0	0.9
HPLC	79	12.6	1.4	2.3	1.0	1.0
Tandem Mass Spec	187	12.0	1.5	2.7	1.1	1.0
Neometrics Accuwell	80	14.2	1.1	2.6	1.6	1.2
Quantase	110	14.5	1.3	2.5	1.6	1.2
Other	90	12.9	0.8	1.9	1.3	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4f. 2002 Quality Control Data
Summaries of Statistical Analyses

LEUCINE (mg Leu/dL whole blood)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 141 - Nonenriched 0 mg/dL whole blood						
Bacterial Inhibition Assays	60	1.3	0.5	0.8	1.7	0.8
PerkinElmer (Wallac)	30	2.4	0.5	0.5	2.3	1.0
HPLC	60	1.8	0.2	0.2	1.7	1.1
Tandem Mass Spec	97	2.1	0.3	0.6	2.1	0.9
Thin-Layer Chromatography	10	1.0	0.0	0.0	1.0	1.0
Other	10	3.1	0.2	0.2	3.2	0.6
Lot 142 - Enriched 3 mg/dL whole blood						
Bacterial Inhibition Assays	69	4.6	0.9	1.0	1.7	0.8
PerkinElmer (Wallac)	29	5.3	0.7	0.9	2.3	1.0
HPLC	58	5.0	0.4	0.7	1.7	1.1
Tandem Mass Spec	100	4.9	0.5	1.1	2.1	0.9
Thin-Layer Chromatography	10	3.8	0.6	0.6	1.0	1.0
Other	10	5.2	0.3	0.3	3.2	0.6
Lot 143 - Enriched 7 mg/dL whole blood						
Bacterial Inhibition Assays	69	7.5	1.4	1.5	1.7	0.8
PerkinElmer (Wallac)	30	9.7	0.8	0.9	2.3	1.0
HPLC	58	9.6	0.9	1.8	1.7	1.1
Tandem Mass Spec	100	9.0	0.9	1.9	2.1	0.9
Thin-Layer Chromatography	10	8.4	0.8	0.8	1.0	1.0
Other	10	7.9	0.4	0.4	3.2	0.6
Lot 144 - Enriched 11 mg/dL whole blood						
Bacterial Inhibition Assays	67	10.6	2.2	2.7	1.7	0.8
PerkinElmer (Wallac)	30	13.7	1.0	1.9	2.3	1.0
HPLC	58	13.8	1.3	2.6	1.7	1.1
Tandem Mass Spec	100	12.4	1.2	2.7	2.1	0.9
Thin-Layer Chromatography	10	11.8	1.0	1.0	1.0	1.0
Other	10	10.0	0.9	0.9	3.2	0.6

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

LEUCINE (mg Leu/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 221 Nonenriched 0 mg/dL whole blood						
Bacterial Inhibition Assays	155	1.3	0.4	0.9	1.3	0.8
PerkinElmer (Wallac)	69	2.2	0.6	0.8	2.2	1.3
HPLC	109	1.6	0.2	0.3	1.5	0.9
Tandem Mass Spec	256	1.9	0.6	0.7	1.9	0.8
Thin-Layer Chromatography	20	0.6	0.5	0.5	0.8	0.9
Other	20	2.6	0.3	0.3	2.9	0.7
Lot 222 - Enriched 3 mg/dL whole blood						
Bacterial Inhibition Assays	157	3.6	0.8	1.7	1.3	0.8
PerkinElmer (Wallac)	66	6.0	1.1	1.5	2.2	1.3
HPLC	109	4.3	0.6	0.7	1.5	0.9
Tandem Mass Spec	255	4.3	0.7	1.0	1.9	0.8
Thin-Layer Chromatography	20	3.4	0.7	0.7	0.8	0.9
Other	20	5.1	0.5	0.5	2.9	0.7
Lot 223 - Enriched 7 mg/dL whole blood						
Bacterial Inhibition Assays	158	7.1	1.5	2.4	1.3	0.8
PerkinElmer (Wallac)	70	11.8	2.1	4.0	2.2	1.3
HPLC	108	7.9	0.5	0.9	1.5	0.9
Tandem Mass Spec	258	7.8	1.5	2.1	1.9	0.8
Thin-Layer Chromatography	20	7.3	0.6	0.6	0.8	0.9
Other	20	8.5	0.7	0.7	2.9	0.7
Lot 224 - Enriched 11 mg/dL whole blood						
Bacterial Inhibition Assays	148	10.0	2.0	3.8	1.3	0.8
PerkinElmer (Wallac)	69	16.3	1.8	3.0	2.2	1.3
HPLC	109	11.7	0.8	1.4	1.5	0.9
Tandem Mass Spec	258	11.2	1.5	2.6	1.9	0.8
Thin-Layer Chromatography	20	9.9	0.7	0.7	0.8	0.9
Other	20	10.2	1.4	1.4	2.9	0.7

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

LEUCINE (mg Leu/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 241 - Nonenriched 0 mg/dL whole blood						
Bacterial Inhibition Assays	74	1.5	0.4	1.0	1.4	0.8
PerkinElmer (Wallac)	40	2.6	0.6	0.8	2.4	1.2
HPLC	50	2.0	0.2	0.7	1.8	1.0
Tandem Mass Spec	185	2.2	0.6	1.0	2.0	0.9
Thin-Layer Chromatography	10	2.4	0.5	0.5	2.4	0.9
Other	10	3.3	0.3	0.3	3.3	0.8
Lot 242 - Enriched 3 mg/dL whole blood						
Bacterial Inhibition Assays	80	3.8	0.5	1.5	1.4	0.8
PerkinElmer (Wallac)	39	5.7	0.9	1.3	2.4	1.2
HPLC	50	4.7	0.3	0.8	1.8	1.0
Tandem Mass Spec	183	4.7	0.9	1.6	2.0	0.9
Thin-Layer Chromatography	10	5.3	0.9	0.9	2.4	0.9
Other	10	5.7	0.5	0.5	3.3	0.8
Lot 243 - Enriched 7 mg/dL whole blood						
Bacterial Inhibition Assays	78	6.9	1.2	2.3	1.4	0.8
PerkinElmer (Wallac)	40	10.7	1.4	1.8	2.4	1.2
HPLC	48	9.0	1.0	1.8	1.8	1.0
Tandem Mass Spec	187	8.2	1.6	2.7	2.0	0.9
Thin-Layer Chromatography	10	9.2	0.8	0.8	2.4	0.9
Other	10	9.3	0.7	0.7	3.3	0.8
Lot 244 - Enriched 11 mg/dL whole blood						
Bacterial Inhibition Assays	68	10.3	1.9	3.5	1.4	0.8
PerkinElmer (Wallac)	40	15.3	1.9	2.0	2.4	1.2
HPLC	49	13.2	1.2	2.0	1.8	1.0
Tandem Mass Spec	189	12.5	2.9	4.4	2.0	0.9
Thin-Layer Chromatography	10	12.8	1.9	1.9	2.4	0.9
Other	10	12.3	1.3	1.3	3.3	0.8

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4g. 2002 Quality Control Data
Summaries of Statistical Analyses

METHIONINE (mg Met/dL whole blood)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 141 Nonenriched 0 mg/dL whole blood						
Bacterial Inhibition Assays	85	0.6	0.8	1.1	0.6	1.2
HPLC	50	0.4	0.1	0.1	0.5	1.1
Tandem Mass Spec	118	0.4	0.1	0.1	0.4	0.9
Thin-Layer Chromatography	10	0.0	0.0	0.0	0.1	1.0
Lot 142 - Enriched 1 mg/dL whole blood						
Bacterial Inhibition Assays	84	1.7	0.8	0.8	0.6	1.2
HPLC	50	1.8	0.2	1.0	0.5	1.1
Tandem Mass Spec	120	1.2	0.2	0.3	0.4	0.9
Thin-Layer Chromatography	10	1.0	0.0	0.0	0.1	1.0
Lot 143 - Enriched 3 mg/dL whole blood						
Bacterial Inhibition Assays	86	4.2	1.0	2.1	0.6	1.2
HPLC	48	3.7	0.5	1.2	0.5	1.1
Tandem Mass Spec	119	3.1	0.4	0.6	0.4	0.9
Thin-Layer Chromatography	10	3.4	0.5	0.5	0.1	1.0
Lot 144 - Enriched 6 mg/dL whole blood						
Bacterial Inhibition Assays	80	7.6	1.5	2.4	0.6	1.2
HPLC	49	7.1	0.7	2.6	0.5	1.1
Tandem Mass Spec	120	5.5	0.6	1.2	0.4	0.9
Thin-Layer Chromatography	10	5.8	0.4	0.4	0.1	1.0

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

METHIONINE (mg Met/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 221 - Nonenriched 0 mg/dL whole blood						
Bacterial Inhibition Assays	148	0.4	0.2	1.5	0.4	1.0
HPLC	82	0.2	0.3	0.4	0.2	0.8
Tandem Mass Spec	275	0.3	0.2	0.2	0.3	0.7
Thin-Layer Chromatography	20	0.0	0.0	0.0	-0.1	0.9
Lot 222 - Enriched 1 mg/dL whole blood						
Bacterial Inhibition Assays	168	1.2	0.6	0.8	0.4	1.0
HPLC	81	0.9	0.7	0.9	0.2	0.8
Tandem Mass Spec	277	1.0	0.6	0.6	0.3	0.7
Thin-Layer Chromatography	20	1.0	0.0	0.0	-0.1	0.9
Lot 223 - Enriched 3 mg/dL whole blood						
Bacterial Inhibition Assays	168	3.4	1.1	1.8	0.4	1.0
HPLC	83	2.5	1.2	1.6	0.2	0.8
Tandem Mass Spec	276	2.4	0.4	0.6	0.3	0.7
Thin-Layer Chromatography	20	2.0	0.0	0.0	-0.1	0.9
Lot 224 - Enriched 6 mg/dL whole blood						
Bacterial Inhibition Assays	160	6.1	1.0	2.3	0.4	1.0
HPLC	83	4.8	1.8	2.2	0.2	0.8
Tandem Mass Spec	274	4.6	0.8	1.1	0.3	0.7
Thin-Layer Chromatography	20	5.4	1.8	1.8	-0.1	0.9

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

METHIONINE (mg Met/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 241 Nonenriched 0 mg/dL whole blood						
Bacterial Inhibition Assays	80	0.4	0.1	0.4	0.5	1.1
HPLC	38	0.4	0.1	0.2	0.5	0.8
Tandem Mass Spec	174	0.4	0.2	0.3	0.4	0.8
Thin-Layer Chromatography	10	0.0	0.0	0.0	0.0	1.1
Lot 242 - Enriched 1 mg/dL whole blood						
Bacterial Inhibition Assays	88	1.5	0.4	0.9	0.5	1.1
HPLC	38	1.3	0.1	0.5	0.5	0.8
Tandem Mass Spec	175	1.1	0.3	0.4	0.4	0.8
Thin-Layer Chromatography	9	1.0	0.3	0.3	0.0	1.1
Lot 243 - Enriched 3 mg/dL whole blood						
Bacterial Inhibition Assays	88	4.1	0.6	1.5	0.5	1.1
HPLC	37	3.2	0.3	0.8	0.5	0.8
Tandem Mass Spec	175	2.8	0.5	0.8	0.4	0.8
Thin-Layer Chromatography	10	3.3	0.7	0.7	0.0	1.1
Lot 244 - Enriched 6 mg/dL whole blood						
Bacterial Inhibition Assays	80	7.1	0.9	1.6	0.5	1.1
HPLC	38	5.5	0.4	1.0	0.5	0.8
Tandem Mass Spec	175	4.9	1.0	1.6	0.4	0.8
Thin-Layer Chromatography	10	6.4	0.5	0.5	0.0	1.1

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4h. 2002 Quality Control Data
Summaries of Statistical Analyses

TYROSINE (mg Tyr/dL whole blood)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 221 - Nonenriched 0 mg/dL whole blood						
HPLC	39	1.1	0.1	0.2	1.1	0.8
Tandem Mass Spec	169	1.0	0.1	0.2	0.9	0.8
Thin-Layer Chromatography	10	0.7	0.5	0.5	0.8	0.8
Other	10	1.8	0.2	0.2	1.8	0.8
Lot 222 - Enriched 2 mg/dL whole blood						
HPLC	50	2.6	0.2	0.5	1.1	0.8
Tandem Mass Spec	170	2.6	0.2	0.6	0.9	0.8
Thin-Layer Chromatography	10	2.4	0.5	0.5	0.8	0.8
Other	10	3.3	0.2	0.2	1.8	0.8
Lot 223 - Enriched 4 mg/dL whole blood						
HPLC	40	4.5	0.2	0.4	1.1	0.8
Tandem Mass Spec	169	4.2	0.4	1.0	0.9	0.8
Thin-Layer Chromatography	10	3.9	0.6	0.6	0.8	0.8
Other	10	5.0	0.3	0.3	1.8	0.8
Lot 224 - Enriched 8 mg/dL whole blood						
HPLC	50	7.4	0.4	1.0	1.1	0.8
Tandem Mass Spec	167	7.5	0.7	1.7	0.9	0.8
Thin-Layer Chromatography	10	6.9	0.6	0.6	0.8	0.8
Other	10	8.1	0.4	0.4	1.8	0.8

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TYROSINE (mg Tyr/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 241 Nonenriched 0 mg/dL whole blood						
HPLC	40	1.1	0.1	0.1	1.1	1.0
Tandem Mass Spec	207	1.1	0.2	0.3	1.0	0.9
Thin-Layer Chromatography	9	2.0	0.3	0.3	1.8	0.8
Other	10	2.0	0.2	0.2	1.9	0.9
Lot 242 - Enriched 1 mg/dL whole blood						
HPLC	40	2.1	0.1	0.3	1.1	1.0
Tandem Mass Spec	207	1.9	0.2	0.5	1.0	0.9
Thin-Layer Chromatography	10	2.6	0.5	0.5	1.8	0.8
Other	10	2.8	0.2	0.2	1.9	0.9
Lot 243 - Enriched 3 mg/dL whole blood						
HPLC	38	3.9	0.3	0.4	1.1	1.0
Tandem Mass Spec	204	3.6	0.7	1.0	1.0	0.9
Thin-Layer Chromatography	10	3.9	0.6	0.6	1.8	0.8
Other	10	4.4	0.3	0.3	1.9	0.9
Lot 244 - Enriched 6 mg/dL whole blood						
HPLC	38	7.0	0.4	0.7	1.1	1.0
Tandem Mass Spec	207	6.3	0.8	1.6	1.0	0.9
Thin-Layer Chromatography	10	6.9	1.5	1.5	1.8	0.8
Other	10	7.1	0.4	0.4	1.9	0.9

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4i. 2002 Quality Control Data
Summaries of Statistical Analyses

VALINE (mg Val/dL whole blood)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 221 - Nonenriched 0 mg/dL whole blood						
HPLC	28	2.2	0.2	0.3	2.2	0.9
Tandem Mass Spec	140	1.7	0.3	0.5	1.6	0.6
Thin-Layer Chromatography	10	1.6	0.5	0.5	1.5	0.9
Lot 222 - Enriched 2 mg/dL whole blood						
HPLC	28	3.9	0.2	0.2	2.2	0.9
Tandem Mass Spec	140	2.9	0.4	0.9	1.6	0.6
Thin-Layer Chromatography	10	3.2	0.4	0.4	1.5	0.9
Lot 223 - Enriched 4 mg/dL whole blood						
HPLC	28	5.9	0.2	0.3	2.2	0.9
Tandem Mass Spec	138	4.1	0.8	1.3	1.6	0.6
Thin-Layer Chromatography	10	5.4	0.5	0.5	1.5	0.9
Lot 224 - Enriched 6 mg/dL whole blood						
HPLC	28	7.5	0.4	0.4	2.2	0.9
Tandem Mass Spec	139	5.5	0.8	1.6	1.6	0.6
Thin-Layer Chromatography	10	7.0	0.7	0.7	1.5	0.9

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

VALINE (mg Val/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 241 Nonenriched 0 mg/dL whole blood						
HPLC	32	2.2	0.1	0.3	2.3	0.9
Tandem Mass Spec	169	1.6	0.3	0.5	1.6	0.7
Thin-Layer Chromatography	10	2.0	0.0	0.0	1.9	0.8
Lot 242 - Enriched 1 mg/dL whole blood						
HPLC	32	3.3	0.3	0.5	2.3	0.9
Tandem Mass Spec	169	2.2	0.3	0.6	1.6	0.7
Thin-Layer Chromatography	10	2.8	0.4	0.4	1.9	0.8
Lot 243 - Enriched 3 mg/dL whole blood						
HPLC	32	5.1	0.2	0.3	2.3	0.9
Tandem Mass Spec	168	3.6	0.6	1.1	1.6	0.7
Thin-Layer Chromatography	10	3.8	0.4	0.4	1.9	0.8
Lot 244 - Enriched 6 mg/dL whole blood						
HPLC	32	7.9	0.4	0.5	2.3	0.9
Tandem Mass Spec	168	5.8	1.2	1.9	1.6	0.7
Thin-Layer Chromatography	10	6.6	0.5	0.5	1.9	0.8

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

TABLE 4j. 2002 Quality Control Data
Summaries of Statistical Analyses

CITRULLINE (mg Cit/dL whole blood)

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 221 Nonenriched 0 mg/dL whole blood						
Tandem Mass Spec	127	0.4	0.1	0.2	0.4	0.7
Thin-Layer Chromatography	10	0.0	0.0	0.0	-0.2	0.9
Lot 222 - Enriched 0.5 mg/dL whole blood						
Tandem Mass Spec	127	0.8	0.2	0.3	0.4	0.7
Thin-Layer Chromatography	10	0.0	0.0	0.0	-0.2	0.9
Lot 223 - Enriched 1 mg/dL whole blood						
Tandem Mass Spec	128	1.1	0.3	0.4	0.4	0.7
Thin-Layer Chromatography	10	0.8	0.4	0.4	-0.2	0.9
Lot 224 - Enriched 2.5 mg/dL whole blood						
Tandem Mass Spec	127	2.1	0.3	0.5	0.4	0.7
Thin-Layer Chromatography	9	2.0	0.3	0.3	-0.2	0.9

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

CITRULLINE (mg Cit/dL whole blood)
- Continued -

Method	N	Mean	Average Within Lab SD	Total SD	Y-Intercept*	Slope
Lot 241 Nonenriched 0 mg/dL whole blood						
Tandem Mass Spec	185	0.5	0.1	0.2	0.5	0.8
Thin-Layer Chromatography	10	0.0	0.0	0.0	-0.1	0.9
Lot 242 - Enriched 0.5 mg/dL whole blood						
Tandem Mass Spec	187	0.9	0.4	0.5	0.5	0.8
Thin-Layer Chromatography	10	0.0	0.0	0.0	-0.1	0.9
Lot 243 - Enriched 1 mg/dL whole blood						
Tandem Mass Spec	185	1.3	0.3	0.5	0.5	0.8
Thin-Layer Chromatography	10	1.2	0.4	0.4	-0.1	0.9
Lot 244 - Enriched 2.5 mg/dL whole blood						
Tandem Mass Spec	187	2.5	1.0	1.3	0.5	0.8
Thin-Layer Chromatography	10	2.2	0.4	0.4	-0.1	0.9

*Estimated by performing a weighted linear regression analysis of mean reported concentrations versus enriched concentrations and extrapolating the regression to the Y-axis.

This ***NEWBORN SCREENING QUALITY ASSURANCE PROGRAM*** report is an internal publication distributed to program participants and selected program colleagues. The laboratory quality assurance program is a project cosponsored by the **Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories.**

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